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SURGICAL TREATMENT OF DIVERTICULITIS OF THE COLON

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Facts potentially useful in the diagnosis and treatment of diverticulitis of the colon were sought in a study of 70 patients in whom that condition was found at operation. Forty were men, and the youngest patient was 39 years old. In 16 the symptoms were acute; in 19 there had been intermittent trouble for years. Symptoms varied, and there were 18 patients in whom none of the symptoms was gastrointestinal. In 14 the preoperative diagnosis had been neoplastic disease of the intestine or pelvic organs. Leukocytosis was present in only half of the patients; the same was true of fever. Gross bleeding occurred in 13. Roentgenologic examination did not always distinguish between presence and absence of inflammatory changes, and in 11 instances the radiologic report was decidedly misleading. In 62 patients the lesion involved the sigmoid colon; in 35 of these it was treated by primary section and anastomosis. The experience of the authors with this operation has been favorable, and they urge that it be carried out, when appropriate, before serious complications can develop.

MOST studies of diverticulitis of the colon come from the large teaching centers. Their leadership in developing a more aggressive and radical approach to the problem is well recognized. No longer is surgical treatment carried out as a last resort, as a life-saving measure, or only when dire complications develop.[1] There is an increasing trend toward offering it early to patients failing to respond to medical treatment.[2] In addition, since the advent of antibiotics and chemotherapeutic agents, an attempt usually is made to remove the diseased segment and not simply to bypass it.[3] Stage operations are seen with ever-decreasing frequency and with progressive shortening of the interval between stages.[4]

Material and Methods

Records of all patients operated on for diverticulitis of the colon at Sacred Heart Hospital from Jan. 1, 1951, to Dec. 31, 1957, were reviewed by us. No attempt at long-term follow-up was made as we were principally interested in accuracy of diagnosis, procedures carried out, and postoperative complications. Seventy patients provided the basis for this study.

Principal locations of the inflamed diverticula were the cecum in 5 patients, transverse colon in 2, entire colon in 1, and sigmoid colon in 62. Since the active disease process which led to operation was confined to the sigmoid colon in the vast majority of patients, it is this group to which closest attention has been paid in this study.

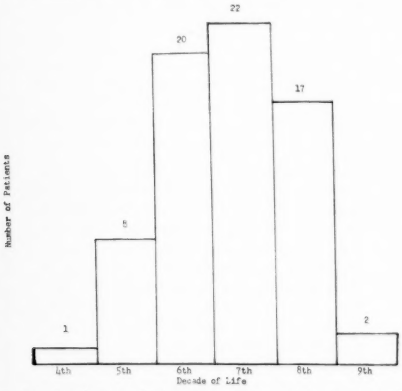
There were 40 men and 30 women. The youngest patient was a man aged 39 with a perforating cecal diverticulum, the oldest an 87-year-old man with

From the Rockwood Clinic.

perforating sigmoid diverticulitis. The distribution of patients according to age is shown in the figure.

Symptoms

In patients whose involvement was in segments of the colon other than the sigmoid, symptoms were, with one exception, acute and of a few hours' to a few days' duration. Patients with sigmoid diverticulitis exhibited considerable variation in the duration of their symptoms. In 16 patients symptoms were acute and measured in terms of hours or days. In 13 patients duration was measured in weeks, in 11 it was measured in months. Nineteen patients had had intermittent trouble for years, manifested in some by vague, ill-defined complaints and in others by recurrent, acute flare-ups often requiring repeated hospitalization. Three patients had no symptoms to suggest the condition, which was discovered at operation.



Age distribution of 70 patients with surgical treatment of diverticulitis of colon.

In patients with lesions of the cecum and transverse colon the uniform complaint was pain localized to that portion of the abdomen containing the disease process, with the exception of one patient with a transverse colon lesion whose symptoms were obstructive in character. One patient with involvement of the entire colon was admitted because of a massive gastrointestinal hemorrhage. Forty-nine of the 62 patients with sigmoid diverticulitis complained of pain, but definite localization was less constant. Other complaints were of constipation, 16, with obstipation in 5; diarrhea, 8 patients; and nausea and vomiting, 7 patients. Thirteen patients had noted the passage of bright blood per rectum; in 9 this was of some magnitude, but in only 4 was it associated with anemia. Four of the patients who had bled had no other complaints whatsoever. Seven patients gave a history of chills and/or fever. In five patients bladder symptoms were predominant. A few patients complained of bloating, weight loss, and general indisposition. Eighteen patients had no symptoms whatsoever referable to the gastrointestinal tract.

Findings

The five patients with cecal lesions had tenderness localized to the right lower quadrant; four had fever; and a mass was noted in one. Both patients with transverse colon lesions had tenderness over the lesion; in one, a mass was palpable. No findings, except pallor, were noted in the 78-year-old man with diffuse involvement of the colon. Two of the patients with ascending colon lesions exhibited leukocytosis. All but two of the foregoing patients were anemic. Four patients had had barium enemas carried out with the following diagnoses: diverticulosis, one; carcinoma of the transverse colon, one; polyp of the cecum, one; ileocecal intussusception, one. Thirty-eight of the 62 patients with sigmoid diverticulitis exhibited lower abdominal tenderness, most marked in the left lower quadrant. In 19 patients a mass was palpable. Fifteen patients exhibited varying degrees of distention. Six were febrile on admission. One patient developed an abdominal wall fecal fistula shortly after admission. Two patients had such fistulas at the time of admission and in one of these patients it was associated with a clostridial wound infection. Two patients had colonic stomas when first seen. In 13 patients no abnormal physical findings were reported.

In 21 of these patients varying degrees of anemia were present, and 31 had elevated leukocyte counts on admission. Proctoscopic examination was carried out in 25 patients, with positive findings in 13. In three patients this consisted only of the presence of blood coming from the upper reaches of the intestine, whereas in the remainder evidence of inflammation and occasionally the presence of diverticula were noted. A plain film of the abdomen was made in 10 patients with the following diagnoses: abdominal mass, 1; intestinal obstruction, 5; negative, 4. A barium enema was carried out in 46 patients with the following diagnoses: diverticulitis, 27; diverticulosis, 10; carcinoma, 3; constricting lesion, 3; extrinsic tumor, 2; and negative, 1. In two of the patients in whom radiologic diagnosis of diverticulitis was made, the possibility of a carcinoma could not be excluded. Among the 11 patients in whom the diagnosis was "diverticulosis" or "negative," 8 were found at operation to have severe, active diverticulitis.

We were interested in learning what the clinician thought he was dealing with before the patient was operated on and also in the accuracy of the surgeon's assessment of the findings at operation. Preoperative diagnoses are shown in table 1. No correct ones were made in patients having lesions of the cecum or transverse colon. Although the condition was known to exist throughout the entire colon in the patient ultimately undergoing colectomy, the source of the bleeding was incorrectly inferred and

a hemorrhoidectomy carried out first. Among patients with sigmoid lesions a correct diagnosis was made or strongly suspected in 61%. One of the patients on whom a correct preoperative diagnosis was made here entered the hospital with a fecal fistula

TABLE 1.—*Preoperative Diagnosis in Seventy Patients with Diverticulitis*

Location of Lesion	Diagnosis	No.	% Correct
Cecum	Acute appendicitis	3	0
	Carcinoma	2	0
Transverse colon	Strangulated periumbilical hernia	1	0
	Carcinoma	1	0
Entire colon	Diverticulitis	1	100
Sigmoid colon	Diverticulitis	29	
	Possible diverticulitis	9	61
	Carcinoma	7	
	Gynecologic disease (ovary 6, uterus 1)	7	
	Acute appendicitis	5	
	Unknown or incidental finding	5	

and a clostridial wound infection resulting from an operation carried out elsewhere on what was thought to be a strangulated inguinal hernia, six days previously.

At the time of operation the correct pathology was recognized by the surgeon in three patients with cecal lesions; in two he thought he was dealing with a carcinoma. The true nature of the condition was apparent in the patients having lesions of the transverse colon and entire colon. Among the patients with sigmoid lesions a correct assessment was achieved in 85%. In four patients the lesion was thought to be carcinoma, while in five the surgeon was uncertain as to the nature of the lesion with which he was dealing.

Treatment

Operative procedures which were performed are indicated in table 2. Among the patients with cecal lesions, right hemicolectomy was carried out in two patients because the lesion was thought to be malignant and in the third because of the extent of the process. Local procedures were utilized when the inflammatory nature of the process was obvious and circumscribed. In both patients with transverse colon lesions, the inflammatory nature was obvious and the extent of the process dictated whether resection or excision was performed. The patient with extensive involvement of the entire colon underwent subtotal colectomy after an ill-advised hemorrhoidectomy failed to curtail his bleeding.

Sigmoid diverticulitis was treated by primary resection and anastomosis in 35 patients. None of these patients had complementary cecostomy or colostomy performed. In only eight patients was the pathological process quiescent at time of operation. In 20 patients marked inflammatory activity was present and 2 of these patients were partially obstructed. In six seriously ill patients abscesses were encountered, and in one patient acute perforation with generalized peritonitis was present.

Stage procedures were carried out in 14 patients. In one instance complementary colostomy was established because of an uncertain anastomosis. In two instances the presence of a large abscess and in one the presence of a clostridial wound infection were the reasons for stage procedures; two of these patients had associated fistulas, as did one other patient in whom a stage procedure was carried out. In five patients the presence of obstruction in a poor-risk patient with active disease was the indication for preliminary decompression. In three instances the true nature of the process was wholly unsuspected, no preparation for an intestinal operation had been carried out, and it was felt unwise to proceed with a primary resection; two of these patients were operated on with a diagnosis of "acute abdomen" and the third because of a mass. The final patient had a ruptured diverticulum, generalized peritonitis, and a gallstone impacted in the terminal ileum.

In four patients local procedures were carried out: in one instance this was done in association with a salpingo-oophorectomy in an effort to relieve low-grade obstruction; in one, after appendectomy, to remove a piece of bone protruding from a perforated sigmoid diverticulum. It was hard to explain the surgeon's choice in the other two patients, in both of whom diverticula were removed, once because of acute perforation and once in association with colporrhaphy and hysterectomy.

Transverse colostomy was performed twice, once in an 87-year-old man with perforation and peritonitis, and once in a 75-year-old critically ill man with severe cardiovascular disease who had obstruction due to his diverticulitis and hemoperitoneum from a bleeding hemangioma of the liver. In the remaining seven patients with sigmoid diverticulitis, although the process was recognized at operation, no procedure conducted directly against it was carried out. In two instances pus was encountered and drainage instituted. Four times diverticulitis was discovered in the course of other operative procedures and because of lack of preparation or history of adequate medical care, a conservative course

TABLE 2.—*Surgical Treatment of Diverticulitis in Seventy Patients*

Segment of Colon Involved	Operative Procedure	No. of Patients
Cecum	Right hemicolectomy	3
	Excision and appendectomy	2
Transverse colon	Resection transverse colon	1
	Local excision	1
Entire colon	Subtotal colectomy	1
Sigmoid colon	One-stage resection	35
	Multiple-stage resection	14
	Local procedure	4
	Colostomy only	2
	Exploration	7

was elected. In one case when coloscopy failed to reveal the source of bleeding from the intestine, the abdomen was closed and the patient's hemorrhoids removed.

In all cases in which tissue was removed the pathologist confirmed the diagnosis of diverticulosis or diverticulitis. In one patient a 3 mm. sessile polyp

also was found to be present, and in another a grade 2, Duke's A adenocarcinoma 1 cm. in diameter was found to be present in the removed sigmoid segment.

Postoperative Course

The postoperative morbidity and mortality are given in table 3. One of the five patients with diverticulitis of the cecum developed mild femoral thrombophlebitis, and one developed a large wound hematoma. The convalescence of the remaining three was uneventful. Both patients operated on for diverticulitis of the transverse colon had an uneventful convalescence. The patient who was operated on for diverticulitis of the entire colon developed an infected wound hematoma and a severe transfusion reaction complicated by jaundice. Among the 35 patients undergoing one-stage resection for diverticulitis of the sigmoid, complications occurred in 7. In one instance the left ureter was injured in the process of mobilizing the acutely inflamed sigmoid; fortunately, the injury was noted at the time of operation, repaired over a T-tube, and caused no further trouble. One patient went into shock postoperatively. One patient was thought

TABLE 3.—*Morbidity and Mortality Among Seventy Patients Operated on for Diverticulitis*

Segments of Colon Involved	No. of Patients	Patients with Postoperative Complications	Deaths
Cecum	5	2	0
Transverse colon	2	0	0
Entire colon	1	1	0
Sigmoid colon:			
One-stage resection and anastomosis	35	7	0
Multiple-stage and other procedures	27	10	2

to have developed a leak in the anastomosis; the process responded well to conservative therapy. There was one instance of ileus and one of small intestine obstruction, both of which responded well to conservative measures. One patient developed transient auricular fibrillation. One patient had to be readmitted because of a mild wound dehiscence. A number of patients were troubled with transient diarrhea and weight loss, but in none did this persist or become a serious problem. Transient mental depression and confusion were occasionally noted in the immediate postoperative period.

Among the 14 patients having stage procedures there was one death. This occurred in a 78-year-old woman on whom a colostomy was performed for acute perforation of a sigmoid diverticulum with generalized peritonitis and in whom an impacted gallstone had to be removed from the ileum at the same time. Three weeks later the diseased segment of the sigmoid was resected. Postoperatively she developed congestive heart failure, the anastomosis leaked, generalized peritonitis developed, and she finally died of a pulmonary embolus on the seventh postoperative day. Complications among the remaining patients included two instances of severe wound infection with abscess formation, one of recurrent fistula, one of small intestine obstruction, one of gangrenous cholecystitis, and one of prolonged urinary retention. Shock followed closure of colostomy in one patient, and another had an unexplained fever for some time. Again diarrhea was occasionally troublesome in the postoperative period. In two of the patients undergoing local procedures recovery was uncomplicated; the course of the other two was febrile, in one associated with the development of a large abscess. Of the two patients on whom transverse colostomy was performed, one, aged 75, died on the 33rd postoperative day of pneumonia which followed atelectasis. The other, aged 87, recovered uneventfully. In those patients in whom nothing was done about the diverticulitis per se at the time of operation no complications occurred, with the exception of one patient who had prolonged urinary retention and syncopal episodes.

Comment

When this clinical study was initiated, we had in mind several questions in regard to the diagnosis and management of diverticulitis, the answers to which we felt were not clear. We do not have a complete answer to each of these questions; nevertheless, we feel justified in presenting certain facts from which, in our opinion, a number of conclusions may be drawn. Diverticulitis, in portions of the colon other than the sigmoid, occurred with such infrequency that it would seem unjustifiable to do more than call attention to the fact that it does occur and is seldom diagnosed before operation.

To discuss the diagnosis of sigmoid diverticulitis might seem elementary, yet we were astonished to find that this diagnosis was not even considered by either clinician or surgeon prior to operation in 39% of the cases we reviewed. An analysis of the reasons for faulty diagnosis brings out the following significant points:

1. Diverticulitis frequently presents a clinical picture mimicking gynecologic disease or carcinoma of the intestine. Others [5] have adequately emphasized concern as to avoiding the pitfall of mistaking sigmoid carcinoma for diverticulitis. To this we heartily lend support, yet in our group of patients no such error was made. Instead, in 14 cases neoplastic disease of the intestine or pelvic organs was the sole preoperation impression, gained, it seems, as the result of a mass being palpable in the lower part of the abdomen or on pelvic examination and in the absence of signs of inflammatory disease. We would urge, as have Bacon and Sherman,[6] the inclusion of sigmoid diverticulitis in the differential diagnosis of such a mass regardless of its size and the absence of local tenderness or systemic evidence of inflammatory disease.

2. In contrast to the above, diverticulitis coli, complicated by perforation, may mimic diseases which produce generalized peritonitis, in particular, appendicitis. Careful clinical examination should help to minimize this mistake, as should keeping in

mind the fact that perforating sigmoid diverticulitis can present abdominal signs elsewhere than the left lower quadrant, as Fallis and Marshall [7] have pointed out.

3. An absence of significant aberration of lower gastrointestinal function should not lead to the exclusion of acute sigmoid diverticulitis from the differential diagnosis. In 18 of our cases (30%) a change in bowel habit had not occurred or was so slight that it seemed insignificant. Colcock [5a] states that 35% of his patients had a change in bowel habit, implying that as many as 65% had no such helpful diagnostic symptom. This is in contrast to Judd and Mears,[8] who report that only 2 out of 68 surgical cases of diverticulitis had no bowel symptoms.

4. Leukocytosis is as frequently absent as it is present in acute diverticulitis of the sigmoid colon, according to our study. This surprising finding is another factor urging us to call attention to the frequency of the noninflammatory character of the clinical picture in many patients. Of the 32 patients in our group whose white blood cell count was 10,000 per cubic millimeter or under, many were acutely ill, and, whereas diverticulitis was diagnosed in most, in 12 of this group it was not suspected.

5. Fever was absent as often as present in patients with acute diverticulitis.

6. Bleeding from diverticula or as a symptom of acute diverticulitis coli has received a good deal of attention in the literature. Gross bleeding was noted by 13 of our patients, but was only one symptom among many except in 4 patients in whom it was the sole presenting complaint. Massive hemorrhage was the chief cause for surgery in two of these patients. Certainly gross bleeding should first of all suggest a disease of the intestine other than diverticulitis. When it does arise from diverticula, it frequently makes the diagnosis extremely difficult.

7. A report from the radiologist indicating the presence of diverticulosis of the sigmoid without evidence of diverticulitis does not mean that significant inflammatory changes are absent. This discrepancy should be recognized by all clinicians and is one of the pitfalls of blind belief in the infallibility of x-ray examination. In 11 instances in our group of patients the radiologic report was decidedly misleading.

We have made no comments concerning the type or location of pain suffered by these patients, inasmuch as we were unable to note any pattern of distress that has not been fully discussed elsewhere. Insofar as treatment is concerned this study deals only with patients operated on. The reader is directed elsewhere for a detailed discussion of indications for operation. Among our patients the indications were, in order of frequency: intractability of symptoms, the presence of a palpable mass, the inability of the radiologist to exclude carcinoma, obstruction, bleeding, and external fistula.

Surgical Procedures.—Surgical procedures may well be considered in three catagories: (1) the elective operation, (2) the emergency operation, and (3) the surprise operation.

When operation is carried out as an elective procedure during a quiescent phase of the disease there is general agreement that a one-stage resection and anastomosis is the procedure of choice.[9] Resection can usually be limited to the sigmoid even though diverticula may be scattered throughout other parts of the intestine. In only one of our patients was it necessary to carry out a subtotal colectomy. In the more complicated case there is no such unanimity of feeling. It is our feeling that a phlegmonous process in the intestine wall, with or without miliary abscesses and extensive local adhesions, low grades of obstruction, severe bleeding, and fistula do not render a multistage procedure mandatory. It should be the condition of the patient rather than the local findings which influences the decision. If the patient is in good general condition and well prepared, it is usually possible to get above and below the diseased segment to achieve a satisfactory anastomosis of comparatively normal intestine. The more radical procedure is sometimes the safer. By adequate mobilization and resection one removes all diseased tissue, avoids tension on the anastomosis, and eliminates the need for subsequent operations with their attendant risks, time loss, and expense. This was the policy followed in 35 of the 62 patients having sigmoid diverticulitis and 5 of the 8 patients with diverticulitis in other portions of the colon. There were no deaths in this group; complications were less frequent and for the most part comparatively trivial.

In the presence of high grades of obstruction, when a large abscess is present which cannot be removed without profound soiling of the peritoneal cavity and leaving behind much devitalized tissue, or when the patient's general condition is poor, obviously a staged procedure offers the only safe approach to the problem. A transverse colostomy will usually allow the inflammatory process to quiet down and keep it quiet as long as the stoma is functioning. This alone may be all that can be done in an extremely poor-risk patient and may offer excellent palliation as far as the diverticulitis is concerned. It is interesting to note that one of our two deaths occurred when a colostomy alone was performed. After recovery from the colostomy, at an interval of two weeks to several months, the diseased segment of intestine may be removed whenever the patient's general condition warrants. If the resection and anastomosis are easily accomplished, many times the colonic stoma may be closed at the same time. If the procedure is difficult, the condition of the intestine leaves much to be desired, and the patient's general condition is poor, closure should be carried out as a third stage. Our only other death occurred in a poor-risk patient in

whom multiple severe complications followed a staged procedure. In general, complications were more frequent and severe in this group of patients.

We were surprised to find a few local procedures still being carried out. In the ascending or transverse colon this may occasionally be adequate. In the sigmoid, where multiple diverticula usually exist, it is difficult to justify attempts to remove individual diverticula. Pemberton and co-workers [3] long ago decried the practice as seldom conducive to lasting relief from disease. Similarly, in two cases with localized peritonitis and abscess, drainage alone was carried out. Both patients survived but in neither, of course, was the basic problem solved.

When acute perforation occurs with spreading or generalized peritonitis, the need for emergency operation is unquestioned, but as to procedure the decision may be difficult. Although acute perforation occurred in four of our patients, it is not common. Pemberton and co-workers [3] reported no instances of acute perforation in 389 cases of diverticulitis. Mayo and Blunt,[9] discussing complications of diverticulitis, found abscess in 57 of 202 cases but no free perforation. Fallis and Marshall [7] reported five deaths with conservative treatment of acute perforation. Exteriorization or extraperitoneal resection would seem to be the logical procedure. However, it is seldom feasible as the mesentery is often short and thick and all the affected intestine cannot be safely brought to the outside. In general, closing or patching with omentum of the perforated diverticulum is the procedure of choice, although sometimes only drainage can be carried out. Needless to say, a transverse colostomy always should accompany procedures of this type. Closure or drainage without complementary colostomy offers questionable security.

Since accurate diagnosis at operation is particularly difficult in the presence of acute perforation, subsequent resection should be carried out not only to remove the diseased intestine but also to avoid the disaster of leaving a carcinoma behind. Immediate primary resection and anastomosis may be done if the patient is seen early and conditions are favorable. Unfortunately, this seldom is the case, but in one of our patients it was done with an eminently satisfactory result.

The surprise operation is performed with distressing frequency. This situation prevails when the first intimation of the correct diagnosis is obtained after the abdomen is opened. Because of lack of proper conception of the problem, the usual routine preparations which have added so much to the safety of elective intestinal surgery have not been carried out. The actual operation finds both the surgeon and the patient unprepared for what should be done. Sometimes, as in the presence of perforation, abscess, or obstruction, the surgeon has no alternative but to proceed boldly and hope for the best. However, in the presence of uncomplicated diverticulitis, be it fulminating or quiescent, a dilemma may present itself. In seven patients in our series the surgeon elected to correct any associated lesions and back out, planning to give the patient a trial of adequate medical therapy and then, if necessary, to reoperate and resect the diseased intestine under more favorable circumstances. However, in most cases where the disease was pronounced, the surgeon faced his problem resolutely and attempted some type of definitive procedure. One can only hope that periodic references to this disease in the literature will serve as a reminder of the frequency of its occurrence and keep "surprises" at a minimum.

Summary

Diverticulitis of the colon is a common condition frequently necessitating surgical treatment. It must be considered in the differential diagnosis of intra-abdominal disease, especially if an abdominal or pelvic mass is present, regardless of the absence of localized or generalized signs of inflammation and regardless of an x-ray report of diverticulosis instead of diverticulitis. In an increasing number of patients the surgical treatment of choice is one-stage resection and anastomosis. In the present series of 70 patients this was carried out in 57% of the total patients with diverticulitis and in 71% of the patients with sigmoid diverticulitis undergoing definitive surgery, with no deaths and minimal morbidity. No longer should this procedure be reserved merely for the uncomplicated or quiescent cases. If recognition and treatment are delayed until serious complications develop, multiple-stage procedures may still have to be carried out.

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SURGICAL MANAGEMENT OF ULCERATIVE COLITIS

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Surgical treatment becomes necessary in a certain number of patients with ulcerative colitis who do not respond to medical management. The operation of low ileorectal anastomosis here described is done a year or more after subtotal colectomy and ileostomy. It consists in mobilizing the rectum, excising part of the rectum with the sigmoid colon, and making an end-to-side anastomosis of ileum to the remaining part of the rectum. During the first few weeks after the second stage, frequent defecations caused considerable disability, but this generally subsided. In 13 patients rectal continence was attained after the first several defecations after the ileoproctostomy; in the remaining one patient incontinence persisted because the sphincter had been damaged by years of preoperative disease. In all cases the anastomosis healed without formation of abscess or fistula. This operation should be considered whenever the rectum and its sphincter mechanism have escaped serious damage, since it offers the hope of avoiding a permanent ileostomy.

The medical management of chronic nonspecific ulcerative colitis is the province of the gastroenterologist. The judicious use of steroid therapy, blood transfusions, certain sulfonamides, and diet under hospital supervision has resulted in satisfactory arrest of the disease in 80% of patients with ulcerative colitis. Surgical management is reserved for those who do not respond to medical therapy. In past years the incalculable morbidity attending the surgical treatment of this disease has led gastroenterologists to defer surgery and to prolong medical treatment despite hopeless odds. This rigid attitude is now being softened by a marked reduction in morbidity that may be attributed to the practice of two principles: "removal of the disease" and construction of a physiological ileostomy.

The absolute indications for immediate surgery are (1) massive uncontrollable hemorrhage, (2) fulminating and diffuse toxic ulcerative colitis, with distention of the colon, (3) perforation with peritonitis, and (4) carcinoma arising in the course of the disease. Elective or probable indications for surgery are (1) unremitting diffuse disease of two or more years' duration, (2) repeated intestinal hemorrhage and persistent anemia or both, (3) diffuse, uncontrollable skin disease (pyodermas), (4) progressive deforming rheumatoid arthritis or spondylitis, (5) ocular disease (iritis, keratoconjunctivitis), and (6) uncontrolled disabling anorectal disease (fistulas, suppurative fissures, abscesses) leading to incontinence. In addition, certain surgical indications are contingent on progression of the disease, such as neurological manifestations like peripheral neuritis or cases of intractable disease in which the patient fails to maintain a satisfactory economic status.

The surgical treatment of ulcerative colitis has been greatly improved and simplified in the last decade. Surgeons now recognize that to effect a "cure" all of the diseased intestine must be removed and that morbidity is lowest for the one-stage colectomy as compared with the older multiple-stage procedures. The lower mortality of colectomy and simultaneous ileostomy in the critically ill patient and in the patient with toxemia, as compared with that of a diverting ileac stoma, is appreciated.

Colectomy is now performed through an incision in the left side of the abdomen, leaving the right side free for the ileostomy and the immediate application of soft, transparent, plastic bags for skin protection (fig. 1). Conventional ileostomy has largely been abandoned in favor of some form of eversion technique [1] with primary suture to the skin, which has resulted in normal small intestinal function within a few days after colectomy. This technique has eliminated the fluid and electrolyte problems and the nutritional failure previously observed during the postoperative period. The rapid return to health and vigor has made the ileostomy more acceptable to the patient, and the development of a variety of ingenious ileostomy appliances and skill in fitting them has done away with much of the danger of corroding the skin.

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New Concept—Ileorectal Anastomosis

The practice of one-stage "removal of the disease" has led some surgeons to extirpate the colon and rectum at one operation. This eliminates forever the possibility of restoring intestinal continuity. In 1956, Aylett [2] reported his experiences with ileorectal anastomosis after colectomy. He pointed out that the success of the procedure depended on the removal of not only the colon but also the rectosigmoid. He further stated that after low ileorectal anastomosis the diseased rectal segment healed.

Follow-up serial biopsy studies revealed mucosal surface healing, although restitution to integrity of the basic architecture of the submucosa could not be expected if it had been scarred by the disease. He presented clinical evidence to show that the lower part of the rectum would not only recover from active disease, but would function adequately as a terminus for the small intestine.

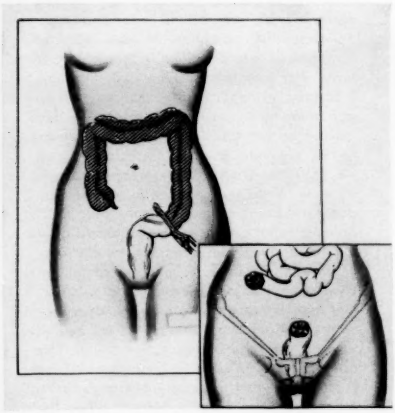

Fig. 1.—First stage of subtotal colectomy and ileostomy.

Aylett's interest in the possibility of ileorectal anastomosis was aroused by his clinical observation that the majority of patients with the diffuse form of the disease had minimal gross involvement of the ampulla of the rectum, while the area immediately above (rectosigmoid and sigmoid colon) was most ulcerated and deformed; e. g., pseudopolyps are often seen first at the rectosigmoid. He postulated that the rectum was least diseased because of its separate nerve supply and that it was kept inflamed by "drip-down" from the suppurative lesions above. Resection of the colon and the rectum down to a point below the deforming disease (about 4 in. above the anus) and mobilization of the lower part of the rectum from the presacral space not only would remove the gross deforming disease but would denervate most of the ampulla as well. Aylett [3a] has had excellent results in 100 patients with diffuse ulcerative colitis who have undergone colectomy with ileorectal anastomoses. His operative technique [3b] has been described in detail. He utilizes a two-stage procedure with a temporary ileostomy above the ileorectal anastomosis.

Since June, 1957, I have performed low ileorectal anastomoses in 14 patients having diffuse ulcerative colitis. The surgical technique differs from Aylett's in that (1) ileorectal anastomosis is done a year or more after subtotal colectomy and ileostomy, and (2) no decompressive ileostomy is done at the time of ileorectal anastomosis. The results so far have been satisfactory, although the number of patients is small and the observation period is short. More time and experience will be necessary for final evaluation, but it appears that the operation has a distinct place in the surgical treatment of this disease.

Technique.—Mobilization and resection of the rectum and sigmoid colon and low ileorectal anastomosis constitute the principal surgical maneuvers. Mobilization of the rectum involves the following procedures: The presacral space is entered medial to the left ureter and in front of Waldeyer's fascia. Sympathetic nerve trunks are preserved on either side. The peritoneal folds at the base of the mesorectum are incised part way down toward the rectovesical pouch or cul-de-sac, and the rectum is brought forward and upward from the sacrum by blunt dissection down to the tip of the coccyx. The middle hemorrhoidal vessels

Fig. 2.—Second stage of resection of sigmoid colon and upper part of the rectum (ileoproctostomy).

are not divided. The anterior peritoneal reflection is thus elevated to a comfortable position where the rectum may be cut across about 2 in. above it, and end-to-side anastomosis with the ileum is made (fig. 2). Important details in the technique are (1) dilatation of the open end of the divided rec-

tum if it is contracted; (2) for the anastomosis, the use of interrupted fine catgut sutures through all layers, and an outside seromuscular approximation with silk: interrupted sutures to avoid stenosis, and absorbable catgut to avoid through-and-through fistulas in the presence of active rectal disease; (3) the pelvis should not be reperitonealized, to allow accumulated blood to drain up into the abdominal cavity rather than to be confined at the anastomosis; and (4) the ovaries in premenopausal women should be sutured with silk to the round ligaments so that they will not prolapse into the presacral space where they may become extraperitonealized and cystic.

Early Results.—The primary disability after ileoproctostomy consists of multiple daily bowel movements which decrease within the first few weeks. The ileum above the anastomosis gradually dilates, as does the rectal ampulla. It is my opinion that more of the terminal ileum, if not diseased, could be saved at the time of colectomy, which would make possible a more solid bowel movement. Six of the patients in this series take antidiarrhea medication.

Aylett [3b] reports no recurrence of proctitis. We have not been so fortunate, although rectal disease present at the time of anastomosis has healed in all but three patients who had persistent disease of the rectum and suppurative cryptitis from three to six months after ileorectal anastomosis. Rectal continence has been well preserved except in the case of one patient who many years previously had sphincter damage and anal fistulas and now wears a pad for occasional leakage. Ileostomy has been reestablished for this reason. In all 14 patients incontinence of the rectum has occurred only for the first several movements after ileoproctostomy.

Sporadic reports of colectomy and ileoproctostomy have been published,[4] but from these accounts we cannot be sure at what level in the rectum the anastomosis has been made. This is most important, since according to Aylett [3] the retention of the involved pelvic colon or rectosigmoid is the principal cause of failure. To clarify this point, I would define the rectum as being 5 in. (15 cm.) in length above the dentate line. Ileorectal anastomosis is made below this level which, viewed within the abdomen at the time of surgery, would be 5 cm. or less above the peritoneal reflection (fig. 2). The lower level of resection would depend on the level of deforming disease, as it must be made below it.

With regard to the healing of the anastomosis between the diseased rectum and the normal ileum, although there was grossly recognizable ulcerative disease at the site of the rectal section all anastomoses performed on patients in this series have healed without formation of abscess or fistula. Care was taken not to spill intestinal contents, and each sigmoid colon was injected with a large volume of 1% neomycin sulfate solution prior to section and anastomosis. An indwelling rectal tube drained any accumulation of pus or stool during the mobilization period. Although the possibility of the development of cancer in the retained rectum must be conceded, I believe it is extremely unlikely since mucosal healing occurs after ileorectal anastomosis.

Failure of Ileoproctostomy.—Of 14 patients in whom ileoproctostomy was done there have been 4 who must be classed as clinical failures. In two the rectal disease has failed to heal. These patients are in moderately poor health and are disabled by frequent small bowel movements. The disease has not become worse nor is the adjacent ileum involved. Both refuse ileostomy. One other patient has already been mentioned as lacking sphincter control. Constant soiling of his perineum resulted in an uncontrolled dermatitis with pruritus, and he was relieved by reestablishment of the ileostomy. The fourth patient, a 15-year-old girl, had previously undergone subtotal colectomy and ileostomy. Much of the terminal ileum was found to be involved with ileitis; nevertheless, ileorectal anastomosis was done about a year later. Persistent ileitis has responded to medical management.

Conclusions

The indications for surgical treatment of ulcerative colitis are unchanged. The postoperative recovery period has been greatly shortened by the use of one-stage procedures and the construction of a physiological ileac stoma. Of the newer surgical concepts, the restoration of intestinal continuity by low ileorectal anastomosis is of particular interest. The results in the 14 cases herein reported indicate that there is a place for this procedure in the surgical treatment of this disease. With hope in sight for the avoidance of permanent ileostomy, the heretofore common practice of total proctocolectomy should be supplanted by subtotal colectomy, whenever the rectum and its sphincter mechanism have not been severely damaged by the disease.

2020 E. 93rd St. (6).

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ORGANIZATION AND OPERATION OF A POISON CONTROL CENTER

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To establish a poison control center means to create an agency that can communicate to a physician, under emergency conditions, the chemical composition of ingested substances and suggestions for diagnosis and treatment. The most important requisite for successful operation is a properly qualified professional person who, by reason of being compensated for his efforts, can devote a sufficient amount of time and energy to the program. Salaries therefore represent the largest items in the budget. Systematic use of the telephone as here described enables the center to function on a 24-hour basis, although at the Cleveland center 97% of the calls have come in between 8 a.m. and midnight. In addition to directly saving lives, the center has done much by means of education to prevent poisonings and serves as an excellent vehicle for improving public relations.

The statistics on accidental poisoning in the United States are grim. Probably close to a quarter of a million children under the age of 5 years ingest toxic or potentially toxic substances each year. Of these, about 300 to 400 will die. Two factors can reduce both of these figures—prevention and prompt, effective treatment. In recognition of this, the physicians of many communities have established poison control centers. It is probable that most communities will, in the near future, want to organize such a center to deal with their problems of accidental poisoning.

In the past five years physicians, and pediatricians in particular, have become acutely aware that accidental poisoning is an important, frequent, and serious problem. A major facet of this problem has been the fact that a great many household products sold to the American public do not give information on their ingredients, toxicity, or effective antidotes. This information is essential to the physician who has to treat cases of accidental poisoning involving these products. With more than a quarter of a million household items being sold and the number rapidly increasing each year, it is clear that the American youngster has potential exposure to substances that may lead to poisoning accidents.

We have, for the past two years, been concerned with the establishment and operation of a poison control center in a large metropolitan community. Previous to that we provided, over an eight-year period, information on poisoning to the medical community under a less formal and organized arrangement.

It appears desirable to record our experiences for several reasons, the most important being the fact that the fundamental principles underlying the establishment of a poison control center and its successful operation do not differ greatly whether the community is small or large. For the most economical use of energy and funds which become available for the establishment and maintenance of a poison control center, it is essential to know what has already been done and what is available and therefore need not be created *de novo* by each center.

Organization of a Poison Control Center

In June, 1957, the Academy of Medicine of Cleveland, with the aid of a grant from the Cleveland Foundation, started a poison control center. The establishment of a poison control center involves the creation of an agency or mechanism by virtue of which the physician, encountering a poisoning accident, can be "plugged-in" to the latest and most authoritative sources of information on the chemical composition of the ingested substances and on diagnosis and therapy.

There are now nearly 200 centers in the United States, and more are being formed. They do not all perform the same service. Some are information-dispensing agencies, others treat victims of poisoning accidents in addition, and a few have a still more complex organization and send trained personnel to follow up each accident with a home visit. Home visits produce data about the accidents which can be, and in some cases are, used to educate the rest of the community as to the nature of the hazard and possible steps that can be taken to avoid or minimize its recurrence.

The Cleveland center, in the first 15 months of its existence, has averaged 8-12 calls per day. Of these calls, 77% are from lay persons. Fifty-two per cent of the calls come between 8 a. m. and 4 p. m. and 3% between midnight and 8 a. m. Of the annual calls, 973 (31%) have involved medicaments, 603 (19%) household products, and 542 (17%) cleaning agents.

From the Poison Control Center, Cleveland Academy of Medicine.

The most important factor determining the successful operation of any poison control center is the acquisition of a properly qualified professional person or persons who can devote a sufficient amount of time and energy to ensure the proper functioning and continuity of the program. We feel that the only way to acquire this time in a reliable and continuing fashion is to pay for it. It is true, and undoubtedly will remain true, that some communities will be blessed with interested persons who will devote the requisite amount of time, for a short period, without remuneration. However, it is our belief that the great majority of communities wishing to establish a poison control center, however small, will not be so fortunate. We would recommend that the primary use of money available for the establishment of a center should be the remuneration of a professional person who will regularly and continuingly devote a definite amount of time to the direction of the center. In the Cleveland experiment, one of the first steps was to secure the services of a medical director and a technical director. Their salaries, and that of a part-time secretary, represent the largest items in the financial aid requested and received for this project.

Duties of a Director.—In small communities, the director may be the embodiment of the center—he will take all calls, will be the repository for the stores of information available, and, perhaps, will act as a consultant in cases of poisoning. In most instances, however, he can be far more effective if his time is spent in organizing and controlling the various facilities needed to operate the center, assembling sources of information, and keeping them up to date. In addition, the director can initiate and supervise programs designed to educate physicians in the proper management of poisoning cases and to acquaint lay persons with the hazards and prevention of accidental poisoning and with the proper utilization of facilities available for the treatment of such cases. The following description of these duties is based on the program at the Cleveland center.

The technical director, a chemist and toxicologist, was appointed to organize material on the vast number of chemical substances included in the formulations of products involved in poisoning. Under his direction, a comprehensive library of books and pamphlets was assembled and kept up to date to provide specific as well as general information about the chemical composition of individual products as information was obtained from many different sources. Community resources were utilized to obtain consultants in various specialty fields, such as botanicals, economic poisons, protective coatings, and industrial chemicals. All these persons are on 24-hour call. If local resources are inadequate, the telephone brings any area of the United States within relatively easy reach for prompt resolution of a special problem.

A medical director, an internist, was appointed to deal with the problems of therapy and with clinical aspects of poisoning. In addition, a group of physicians with highly specialized interests is available for consultation.

Facilities.—Poisoning accidents are emergencies which may arise at any time and which require immediate attention. At this center, dialing a well-advertised telephone number connects the caller with the operator at the Academy of Medicine's 24-hour call service. This operator will, through a direct line to the University Hospitals, contact the resident physician on call for poisoning cases. At this hospital, members of the senior resident staff of the pediatrics service rotate through the duties of poison control officer as an integral part of their training. In every case the operator gets the name, telephone number, and agent involved and ascertains whether the patient's private physician has been called. This information is taken while the operator is awaiting the poison control officer's answer. Every effort is made to have the patient contact his private physician, and his call is put through to the poison control officer only when the private physician cannot be located or in cases in which urgency is apparent or in cases in which the caller has no private physician. An advantage of routing all calls through the Academy of Medicine telephone service is that these operators are skilled in locating physicians and can be doing this while the patient is speaking with the poison control officer or is on his way to a hospital emergency room.

The sole function of the poison control officer is that of supplying information. To this end, a complete library of books, pamphlets, and memorandums on poisoning is kept in one or more strategic locations in the hospital. A list of these books has been published.[1] At the Cleveland center, the poison control officer has other hospital duties which keep him in the vicinity of a telephone in an outpatient department office during the day. This telephone is a special line, used only for calls on poisoning, so that there will be no hold-up due to busy hospital lines. The major, and most complete, library of information is kept in this outpatient department office, since the vast majority of calls come during the day. After 4 p. m. the poison control officer is either at Babies and Childrens Hospital, where he can readily use the main library, or else he is in the hospital emergency room or in his living quarters. Duplicates of the most useful sources of information have been placed in each of the latter two places. If the poison control officer is not near the special telephone, the Academy of Medicine's call service operator can call the University Hospitals on a private trunk line that eliminates delays. From the hospital, where a Telepage call system is used, the poison control officer is called as "Doctor Pico" (abbreviation for poison information center officer). By using this system, the operator need not know

the name of the current poison control officer. Furthermore, should the latter not respond to his call other physicians will call in and take over.

Cuyahoga County covers a large metropolitan area of northeastern Ohio. Physically it was not practical and professionally it was undesirable to have one center in this area. However, the problem of prompt, effective treatment of poisoning accidents is a real one. Recognizing this need, the Academy of Medicine center urged the respective staffs of the local hospitals to create treatment centers at their hospitals. These treatment centers are under the supervision of a visiting physician and are primarily designed for therapeutic activities. Nineteen local hospitals instituted this program, generally under the aegis of a pediatrician. Periodic meetings have been held by this group and the professional staff of the center to discuss mutual problems and recent advances. A protocol for treating a poisoning emergency was drawn up by this group and made an integral part of the respective hospital's procedure. A poison therapy cart has also been described.[1] At a recent meeting it was suggested that another visiting physician be added to the treatment center's staff at each hospital so that an internist and a pediatrician would be available for consultation. Each visiting physician, in addition to consulting with the resident staff on specific problems as they occur, arranges periodic staff meetings to discuss the many problems attendant on proper and effective therapy for victims of accidental poisoning. These meetings generally center about a recent particular local poisoning case and serve to educate the house and visiting staff.

Consultants and Special Facilities.—The efficacy of the poison control center can be significantly increased by use of the technical resources of the community it serves. Thus, it would be well to know the nearest location of an artificial kidney and of a laboratory wherein chemical analyses of body fluids can be done on an emergency basis. In the industries, schools, museums, and health departments of a community, persons can be found who will willingly serve, on a 24-hour basis, as helpful consultants on the identification of botanicals, paints, cleaners, medicaments, and industrial and agricultural chemicals. Such a group of consultants has been invaluable in the operation of this center.

Educational Activities

The circumstances surrounding poisoning accidents are strikingly similar and are such as to convince one that a program designed to educate those who supervise the activities of children under 5 years of age would return a handsome dividend in lives saved and illness prevented. Such a program involves the continuing and repetitive education of medical people, such as physicians and nurses, as well as of nonmedical persons, such as parents, baby sitters, firemen, and policemen. The outline of the educational program sponsored by the Cleveland center, given below, is a guide to what can be done. It should be apparent that this venture consumes time, money, and energy and may well be beyond the immediate objective possible for any such poison control center unless cooperative and collaborative efforts can supply the center with educational material so essential for an educational program.

Education of Physicians.—The following items are included in the educational program for medical people: 1. Lectures, conferences, and clinical-pathological exercises are designed to bring out the problem of poisoning, its diagnosis, its pathological physiology, and its therapy. 2. Articles on poisoning, published in a journal having wide circulation among the local practitioners, are used. The Cleveland center has published articles on the general aspects of poisoning and its therapy and on specific poisonings (salicylate, lead) in *The Bulletin of the Cleveland Academy of Medicine*. The National Clearinghouse for Poison Control Centers puts out an excellent monthly bulletin on the various aspects of poisoning which is distributed to local physicians in charge of treatment centers. 3. Meetings between the professional staff of the center and the physicians representing the local hospitals provide a great deal of mutual education in the way of new therapies, pertinent publications, and interesting cases encountered. 4. Reprints and abstracts of pertinent articles are prepared at the center and distributed to the participating hospitals and, through the latter, to any interested physician. 5. Some pharmaceutical firms publish excellent brochures on the various aspects of poisoning; these are obtained by the center and distributed locally.

Education of Nonmedical People.—Education of nonmedical people involves the following procedures: 1. The physician has an important role in educating the public to the prevention and proper treatment of poisoning. He can place literature in his waiting room. He has the unparalleled opportunity repetitively to bring up the topic of prevention of poisoning accidents to patients who care for small children. When prescribing medicaments, he can stress proper safeguarding and disposal when the drug is no longer needed. By being willing to lecture on this topic to the Parent-Teachers Association and similar groups, he can reach a much larger audience. 2. Pamphlets can be distributed through physicians' offices, pharmacies, visiting nurses, and well-child clinics. A folded, 8-by-11-in., red, black, and white pamphlet on the danger of household preparations was designed at this center. Its theme was "out of sight, out of reach helps keep your child out of trouble." More than 100,000 of these pamphlets have been requested in the past two months. 3. The Cleveland center helped organize and sponsor a poster contest for school children, in cooperation with the Cleveland Board of Education and the Catholic Board of Education. The

winning posters have been used to alert parents to the problem of accidental poisoning. These are effective in outpatient departments and other waiting rooms. 4. A Cleveland television station, KYW, as a public service produced and put on, as part of the center's local educational program, a 30-minute television program entitled "Antidote." Professional actors were used, and the poison control center staff served in a consultative capacity. A kinescope of this program was made for future use. 5. Lectures to parent-teacher groups and to baby-sitter groups become a frequently requested item when education about poisoning is undertaken in a community. At this center there is in preparation a speaker's kit containing suitable visual aides, a subject-material outline of a 30-minute talk, and pertinent reference material. 6. Other items include newspaper articles on poisoning, which reach a wide segment of the population and can be timed to coincide with an expected increase in the incidence of a particular type of poisoning, e. g., availability of insecticide poisons during the summer months. Recently, the *Sunday Cleveland Plain Dealer,* which is the only local paper read that day by over half a million people, devoted half of the front page to a description of the poison control center. Another newspaper article, by Mrs. Helen MacDonald, was printed in *The Baby Bulletin* and distributed to 20,000 mothers of preschool-aged children. Other articles have appeared in the Ohio Bell Telephone Company's "Hello" leaflet (circulation of 1,500,000), the *General Electric Company Bulletin,* various hospital newspapers, and the *University Center Bulletin.* Information provided for firemen and policemen is usually put to good use: the simple request, directed to a chief of police, that, when poisoning victims were brought to a hospital by his officers, the container also be brought along has greatly expedited the identification of poisons.

Use of Community Organizations.—It was an enlightening and fruitful experience to discover that there are many active community organizations which are willing—indeed, eager—to disseminate educational material on poisoning. We cannot emphasize too strongly how superbly the problem of poisoning prevention is suited as a vehicle for furthering the relationship between the medical profession and the public it serves. The following agencies have been of inestimable assistance in implementing and supporting the programs of the Cleveland poison control center: the Cleveland Foundation, the Greater Cleveland Safety Council, the Northeastern Ohio Pediatrics Society, the Visiting Nurse Association, and the Cleveland Division of Health.

National Clearinghouse for Poison Control Centers

It will be apparent to anyone who organizes a poison control center that the items necessary for its operation could be used by any center in the United States. For example, a single series of articles on poisoning, particularly if prepared by authorities on the several aspects of the problem, meets the needs of all centers. It is pathetically wasteful of time, available money, professional talent, and effort for each center painstakingly to accumulate its own card file of chemical compositions of trade-name products, abstracts of the current literature, new drugs and their evaluation, television programs, radio scripts, pamphlets, publicity releases, and other such items. In recognition of this problem and the need for leadership in coordinating and interdigitating these individual efforts, the National Clearinghouse for Poison Control Centers was established, under the direction of Howard M. Cann, M.D., in 1957, as a branch of the U. S. Public Health Service, Division of Special Health Services (Accident Prevention Program), Department of Health, Education, and Welfare. With this leadership, it is hoped that resources can be brought to command the best available talent to produce materials which local poison centers could utilize effectively. Instead of well-intentioned local amateurs—and this includes our own group—spending time, money, and energy to produce amateur material, such a central agency should be able to produce professionally expert material which would serve the needs of all centers. Thus, the reduced costs of this material to the individual center would make it possible to use such money as may be available for reimbursing a qualified person to act as a director and, if possible, to provide him with some clerical or secretarial assistance.

Summary

A program for the establishment of a unit for dealing with the problem of accidental poisoning in a community includes a mechanism whereby physicians and patients can be provided with immediate information and assistance to insure effective and definitive therapy of poisoning accidents. Such an educational program, directed at physicians and the general public, has a prophylactic value. The success of such a program depends on two factors: (1) securing the services of qualified personnel and remunerating them adequately and (2) provision, through the cooperative efforts of all parties interested in the prevention of accidental poisonings, of high-caliber technical and educational material which could be used by any community establishing a poison control center.

2009 Adelbert Rd. (6) (Dr. Herman).

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A complete list of references may be obtained from the authors.

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TECHNIQUE, HAZARDS, AND USEFULNESS OF PERCUTANEOUS SPLENIC PORTOGRAPHY

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and
Louis M. Rousselot, M.D., New York

Percutaneous splenic portography is the diagnostic injection of a radiopaque solution into the spleen. This is done with the patient under general or local anesthesia, and the solution is delivered rapidly into the splenic pulp as near as possible to the hilum; a series of roentgenograms is then made at 2, 4, 6, 8, 12, 16, 24, and 32 seconds from the start of the injection. The technique here described includes many essential precautions and yields manometric data on the pressures existing within the spleen and portal system. Experience with 266 portograms has enabled the authors to anticipate possible difficulties and complications and has demonstrated the value of diagnostic information so obtained in cases of disturbed portal circulation.

Percutaneous splenic portography is a procedure which yields diagnostic information essential to both the medical and surgical management of patients in whom there is presumptive clinical evidence of alterations in the portal venous system. Its major usefulness has been the establishment of definite anatomic and pathophysiological criteria for the diagnosis of portal hypertension. Extent of "extrahepatic collateralization," major vessel size, presence or absence of portal and/or splenic vein thrombosis, and compression or invasion of major portal radicles may be well demonstrated (fig. 1*A*, *B*, and *C*). Postsurgical evaluation of portacaval anastomosis may also be derived from the procedure (fig. 1*D*).

Prompted by reports from European and Latin American investigators,[1] one of us (L. M. R.), in 1952,[2] performed what is believed to be the first percutaneous splenic portogram in the human in the United States. We have since had experience with 266 portograms, 172 of which have been multiple-exposure serial percutaneous splenic portograms.

There have been numerous reports concerning the diagnostic worth of the procedure [3]; however, few have given more than an abridgement of the full details of the technique. It should be emphasized that inherent dangers exist and may be experienced in an appreciable number of instances if proper attention to several details is not observed. A lack of familiarity with these details has been, in our opinion, responsible for failure, as well as bringing discredit to the procedure. Because of our own rewarding experience and increasing requests for particulars of the technique of splenic portography, we feel this detailed report on 172 serial splenic portograms may have merit.

Certain aspects of technique vary in different clinics. The following recommendations have evolved from extensive experience with the procedure on the surgical and radiological services of St. Vincent's Hospital, New York City, since 1952. It is felt that adherence to these basic principles will continue to contribute valuable diagnostic and investigative data. In addition, morbidity will probably be kept at a minimum.

Clinical Assistant Surgeon, St. Vincent's Hospital, and Instructor in Surgery, New York University College of Medicine (Dr. Panke); Assistant Attending Radiologist, St. Vincent's Hospital (Dr. Bradley); Associate Research Surgeon, St. Vincent's Hospital (Dr. Moreno); Director of Radiology, St. Vincent's Hospital, and Professor of Clinical Radiology, New York University College of Medicine (Dr. Ruzicka); and Director of Surgery, St. Vincent's Hospital, and Professor of Clinical Surgery, New York University College of Medicine (Dr. Rousselot).

Preparation for Procedure

Timing.—Percutaneous splenic portography is now an elective diagnostic tool. The procedure is performed when indicated, whether or not the necessity of eventual surgery has been established. Occasionally, as in emergency cases, the examination is done immediately before operation. More often, it is carried out days in advance of any proposed operation, as part of the diagnostic investigation. Not infrequently portograms are obtained after surgery, for example, in evaluating portacaval anastomosis.

Contraindications.—Contraindications to portography are (1) marked alteration of the blood-clotting mechanism, (2) history of allergy, (3) inability of the patient to cooperate (a contraindication that usually refers to the comatose or precomatose patient with excessive involuntary respiratory excursions), and (4) known tumors of the spleen (rare).

Preparation of Patient.—The patient should be hospitalized. Prothrombin time, bleeding and clotting time, and platelet count are routinely checked. Full instruction to the patient relative to what he will experience and the importance of his control of respiration should be given in considerable detail the day before the procedure and again immediately prior to it. Written permission for portography is obtained. The patient is permitted to take

nothing by mouth after midnight of the evening preceding portography. If the procedure is to be done in the afternoon, a liquid breakfast is allowed.

Sterilization of the colon is attempted in elective cases because of the possibility of puncturing the splenic flexure. One gram of neomycin is given every four hours for 24 hours prior to portography. A colon irrigation is performed prior to the procedure. An intravenous sensitivity test is performed, using 1 cc. of dye, either the day before or some hours prior to the precedure.

A barbiturate, plus meperidine (Demerol) hydrochloride, and atropine are administered in dosages according to the size and general condition of the patient. These are given, in essence, for premedication prior to the use of local (1% procaine

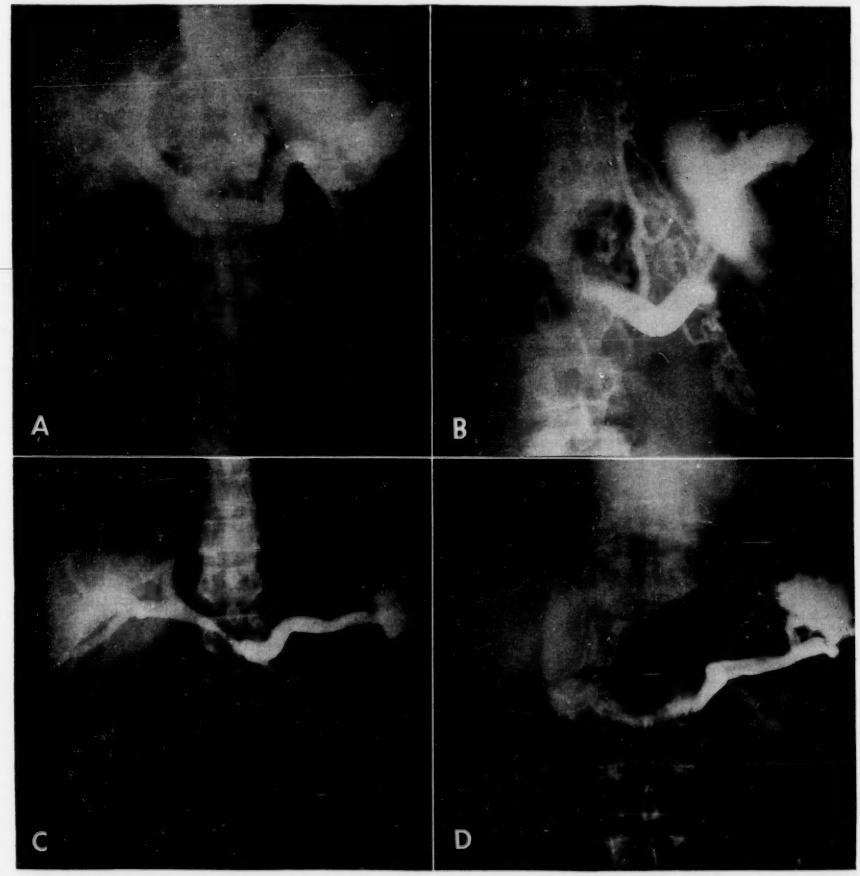

Fig. 1.—*A*, splenic portogram showing "extrahepatic collateralization" in patient with Laennec's cirrhosis and portal hypertension. Note large, naturally occurring, spontaneous portal-systemic shunt arising from left main branch of portal vein and coursing downward to enter vena cava. Shunt did not prevent development of esophagogastric varices which bled massively. Direct end-to-side portacaval shunt was performed successfully. *B*, splenic portogram demonstrating lack of visualization of portal vein in patient with bleeding varices and massive ascites. This was interpreted as thrombosis of portal vein (later confirmed at autopsy). *C*, splenic portogram demonstrating compression and invasion of portal vein from carcinoma of head of pancreas. *D*, splenic portogram demonstrating open, functioning end-to-side portacaval anastomosis seven years after operation for bleeding esophagogastric varices.

infiltration) anesthesia. Local anesthesia is our preference in the adult, whereas, in children, anesthesia induced by tribromoethanol (Avertin) has proved most satisfactory. Diphenhydramine (Benadryl) hydrochloride is also given intramuscularly to minimize the possibility of allergic phenomena. If general anesthesia is to be used, the choice of method of premedication is usually left to the discretion of the attending anesthesiologist.

Equipment.—The equipment (sterile) necessary for carrying out the procedure consists (fig. 2) of four towels, three stainless steel cups for solutions, two 20-cc. syringes, one 50-cc. syringe, three three-way stopcocks, two 25-gauge hypodermic needles, two 19-gauge spinal needles, 6-in. rubber or plastic connecting tube, B-D special flexible connecting

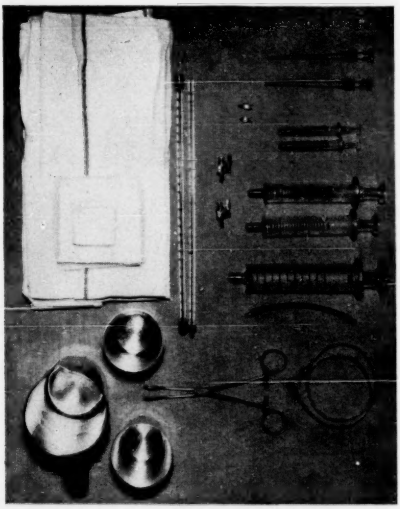

Fig. 2.—Equipment used for performing procedure of combined splenic pulp manometry and splenic portography.

tube (with Luerlock connection) for roentgenography, 2-by-2-in. gauze pads, water manometer, 1% procaine solution, tincture of thimersol (Merthiolate) (1:1,000), isotonic sodium chloride solution, and 50 cc. of 70% solution of sodium acetrizoate (Urokon sodium).

Procedure

The procedure is performed in the x-ray department. It is advisable to clean the table with a suitable antiseptic solution or soap and water rinse just prior to portography to minimize the possibilities of bacterial contamination. Lead shielding is used to prevent scatter irradiation and exposure of films during the manually performed serial roentgenographic examination. Gonadal shielding is used in children and in adults up to the age of 40.

The patient lies supine on the x-ray table. The left arm is raised above his head; the right arm is placed at the side. Blood pressure and pulse rate are recorded.

A scout film is taken, centered at four finger-breadths below the xiphoid, primarily to check exposure factors and position of the patient. It is also useful as a plain film for subsequent interpretation of the portogram.

Fluoroscopic examination in the anteroposterior projection then determines the approximate level of the splenic hilum. This point is marked on the thorax.

A wide skin preparation with use of either tincture of thimersol or hexachlorophene (pHisoHex) is made. The left side is then suitably draped with sterile towels. Several thicknesses are used to cover the x-ray table in the immediate area. Care must be taken to avoid the saturation of these towels with saline solution and blood, since the table may be soiled with pathogenic organisms which might diffuse through wet towels and contaminate equipment during the procedure.

In order to minimize the possibility of inoculation of micro-organisms during splenic puncture, precautions rigidly adhered to are (1) use of cap and mask by the operator, (2) placement of a sterile towel over the field during fluoroscopic examination and while x-rays are being taken, and (3) avoidance of multiple personnel passing by the sterile setup used for the procedure.

The topographic site for splenic puncture is then selected. This site may vary, depending on the spleen size and habitus of the patient, but the most commonly used location is the ninth intercostal space in the posterior axillary line. As stated above, the scout film of the abdomen and fluoroscopic examination are helpful in selecting the target site. Local infiltration is carried out with use of 1% solution of procaine, or general anesthesia is administered, as in children.

Fifty cubic centimeters of 70% solution of sodium acetrizoate is drawn into a 50-cc. Luerlock syringe. The syringe is then attached to a special flexible plastic connection with Luerlock adaptors (Becton-Dickinson). This plastic tubing is then filled with solution from the syringe, and the unit (syringe and tubing) is set aside, pending manometric readings.

The patient next is carefully instructed regarding avoidance of excessive respiratory excursions during the time the needle is in the spleen. This is most apt to occur after the periods of voluntary apnea which must be maintained during actual insertion of the needle as well as during changes of connections. The patient should be warned that transitory left upper quadrant, transabdominal, or

left shoulder pain may occur and should be cautioned against motion while the needle is in place, even though pain may be felt.

Splenic Puncture.—The patient is asked to stop breathing in the midpoint of a respiratory excursion, and an 18-gauge spinal needle with stylet is introduced. The direction of the needle will depend on the estimated location of the splenic hilum. Occasionally, the capsule of the spleen will be felt as a point of resistance, but this is by no means a constant experience. Once the splenic pulp has been reached no resistance will be encountered. The needle is then advanced 1 to 2 cm. into the splenic pulp. When splenomegaly is present, the needle preferably should be advanced further so that the dye may be deposited closer to the hilum of the spleen (at a point approximately 3 to 4 cm. from the hilum).

The stylet is then removed, and the patient resumes normal breathing. A slow drip of blood usually confirms the intrasplenic location of the needle, but occasionally a splenic pulp thrombus will obstruct such flow. The rate of the drip usually varies directly with the portal tension.

Manometric Readings.—A water manometer is then connected to the needle, with a short length of tubing (rubber or plastic) interposed to avoid a rigid system and thereby minimize the possibility of splenic laceration (fig. 3*A*). Apnea is maintained only during the few seconds necessary to complete the connection. Any possible thrombi are then cleared by the injection of 1 or 2 cc. of saline solution, and the first of three sequential manometric determinations are then measured. The average of the three readings is used as the near index of actual pulp pressure. The pressures are taken with the zero point of the manometer at table level and are corrected to a base line by subtracting 12 cm. from the reading. This figure is the average distance from the table to the level of the anterior bodies of the first and second lumbar vertebrae as measured in 52 adult cadavers.

Dye Injection.—Again, voluntary apnea is resumed while the manometer is disconnected and the dye-filled syringe attached via the flexible connecting tube (fig. 3*B*). Normal breathing is then permitted. A sterile towel is placed over the field. Fluoroscopic examination is again carried out during a test injection of 5 cc. of dye. If necessary, the position of the needle is readjusted to minimize subcapsular dye extravasation with its associated pain and inefficient dye uptake. It is our belief that more than two trial splenic punctures are inadvisable. When it has been established fluoroscopically that the dye deposit about the needle tip is in the proper position within the splenic pulp and that there is visual evidence of good flow across the splenic vein, a manually operated cassette changer is brought into position. An automatic changer is preferred by some, but film size is usually limited. Forty cubic centimeters of sodium acetrizoate then is injected rapidly (8 to 12 seconds). The 14-by-17-in. films are manually shifted through the Bucky slot and exposed at 2, 4, 6, 8, 12, 16, 24, and 32 seconds from the start of injection. The first six films best demonstrate the extrahepatic portal system and the intrahepatic vasculogram. Later films have been taken for our study of the hepatogram phase but are not necessary for routine diagnostic use. A single film is difficult to interpret and may at times be entirely misleading. The needle is removed as soon as the injection is completed, again during a very brief period of apnea.

After-care.—The patient is then returned to his room and kept at bed rest until the following morning. Vital signs are checked frequently. Diet is restricted to fluids until the next morning.

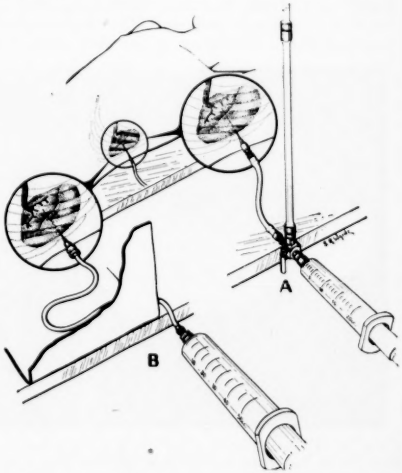

Fig. 3.—*A*, splenic pulp manometry. Water manometer is attached to intrasplenic needle with length of plastic or rubber tubing interposed to avoid rigid system. Zero level of manometer is at table level and is later corrected to level of anterior upper vertebral bodies (average: 12.0 cm.). *B*, rapid injection of 40 cc. of 70% solution of sodium acetrizoate. Use of special Leurlock plastic connecting tube avoids rigid system and prevents "blowouts" during injection. Lead shielding has been placed to avoid exposure of films as they are rapidly shifted through manually operated cassette changer.

Complications

Allergic Reactions.—We have to date experienced no serious reaction to the intrasplenic injection of sodium acetrizoate. A transient bradycardia and mild elevation of arterial blood pressure are frequently noted but have been of no serious consequence.

Pain.—Pain may be absent to severe but is experienced in some mild degree in a majority of patients. It is usually described as a pressure or burning sensation and may be localized in the left upper quadrant or may radiate to the left shoulder or across the upper abdomen. It is usually transitory but occasionally may persist as a dull ache in the left upper quadrant for as long as seven days.

Bleeding.—Bleeding requiring transfusions of 500 cc. (three cases) to 2,000 cc. (one case) has occurred in 2% of the cases. In these cases, multiple splenic punctures (more than two) had usually been performed and are now avoided. In no instance has laparotomy been required.

Infection.—Pyrogenic reactions occurred in 2% of our cases. If organisms are inoculated during injection, a sepsis may conceivably occur. If infection is secondary to puncture of a viscus, a localized peritonitis may result. In either instance appropriate antibiotic therapy is instituted. Our single fatality occurred 48 hours after an unsuccessful attempt at splenic portography which had been immediately preceded by a splenic biopsy with a needle from a separate set. The cause of death was a fulminating Welch's bacillus bacteremia. Postmortem examination disclosed a primary endothelioma of the spleen as the cause of splenomegaly. Three patients exhibited severe pyrexia two to four days after the procedure. Blood cultures in all instances were sterile. Other systemic manifestations were absent. All responded to antibiotics.

False Puncture.—False puncture occurred in 2% of our cases. If proper precautions are not taken, the point of the needle may be extrasplenic and dye may be deposited in the free peritoneal cavity or into adjacent viscera. In the former instance, the dye will gravitate to the pelvic floor when the patient assumes an erect position. Pelvic pain and urinary urgency may be experienced. These symptoms are of short duration as the dye is rapidly absorbed. The opaque medium may also gain access to the free peritoneal cavity by escaping from the pulp backward along the needle tract. This is more likely to occur in normal-sized spleens. We have noted dye free in the peritoneal cavity in only two instances (fig. 4A). In our series there have been two instances of inadvertent puncture of adjacent viscera—in one case, the kidney (fig. 4*B*), and in the other, the left hepatic lobe (fig. 4*C*). No morbidity resulted.

Thoracic Complications.—The lower confines of the left pleural space are frequently traversed during the procedure. A transitory chemical pleuritis, usually without systemic manifestations, may result as revealed by an audible friction rub. We have recognized this complication in only two patients. Pneumothorax is a remote possibility which has not yet been encountered.

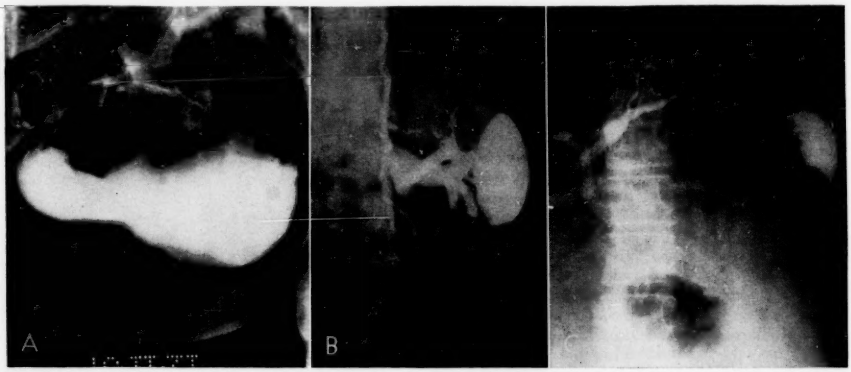

Fig. 4.—*A*, demonstration of dye free in pelvis secondary to accidental extrasplenic injection. *B*, false puncture into left renal parenchyma. Left renal and vertebral veins are filled with dye. *C*, false puncture into enlarged left hepatic lobe. Main portal vein is seen partially filled with dye, showing hepatofugal flow in case of portal hypertension.

Failure Rate.—We have failed to obtain successful portograms in eight (5%) of our cases. These failures have usually been experienced by trainees. When the procedure has been repeated in the same patient by a more practiced operator, success has always been realized.

Summary

Percutaneous splenic portography is a valuable aid in assaying the portal venous system. Inherent dangers of the procedure must be realized. Adherence to minute details of technique should minimize these hazards. Previous reports have described only an abridgement of these details, which are vital to the successful performance of portography. The risk of the procedure should be

considered acceptable in view of the vital information gained concerning the usually serious lesions affecting the portal circulation.

170 W. 12th St. (11) (Dr. Rousselot).

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PERINATAL MORTALITY IN THE NORTH CAROLINA MEMORIAL HOSPITAL, 1952-1958

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An audit of perinatal deaths (from birth through the 28th day) was made by reviewing the mother's and infant's charts and the autopsy records for a series of 2,728 deliveries in a university hospital. During the period of the study, the perinatal mortality was reduced from 38.67 to 23.39 deaths per 1,000 births for infants weighing 1,000 Gm. or more. This was partly explained by a progressive decrease in the proportion of indigent patients during the period of study, for striking contrasts were found between the causes of death reported for private patients and those for unregistered patients. Possible errors in obstetric and pediatric management were sought for. The most frequent errors in obstetrics leading to perinatal deaths related to the management of fetal distress and of toxemia of pregnancy. The major problems of the neonatal period, as judged from autopsy findings or clinical diagnoses in 63 cases of neonatal death, were prematurity (26 cases), birth injury (13 cases), and infection (9 cases).

It is important to make an audit at periodic intervals to determine the progress of an obstetric service. It is appropriate to make an analysis of the perinatal mortality at the North Carolina Memorial Hospital at this time, since the Obstetrical and Gynecological Department of the University of North Carolina has just completed its fifth year as a service.

Perinatal mortality in this study refers to all deaths of infants weighing 400 Gm. (1 lb.) or more through the 28th day of life. Immature refers to infants weighing 400 to 1,000 Gm. (1 to 2¼ lb.); premature refers to infants weighing 1,000 to 2,500 Gm. (1¼ to 5½ lb.); and mature refers to infants weighing 2,500 Gm. or more. Records of the North Carolina Memorial Hospital, the North Carolina State Health Department, and the nurseries for premature infants at Duke University and the University of North Carolina were reviewed in order to obtain accurate data as to the number of perinatal deaths. Each fetal and neonatal death was studied by review of the mother's and infant's charts and of autopsy records. (Autopsies were performed in

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Read before the Annual Meeting of the North Carolina Obstetrical and Gynecological Society, Mid Pines, N. C., April 19, 1958.

92.5% of all of the fetal and neonatal deaths.) The pertinent data were recorded on a special study sheet for tabulation.

General Data and Causes of Death

Table 1 shows the number of deliveries each year, the perinatal mortality by birth weight, and the rank of the North Carolina Memorial Hospital among the state's 207 hospitals with obstetric services. It is evident that there has been a yearly increase in the number of deliveries as well as a significant reduction in the perinatal mortality in 1956 and 1957. There are probably two explanations for this reduction in fetal and neonatal mortality. The service has had a progressive increase in the number of private patients and university students' wives; both of these groups have a relatively low

TABLE 1.—*Perinatal Mortality at North Carolina Memorial Hospital, 1952–1958, with State Average and Hospital Rank*

	Deliveries, No.	Perinatal Mortality per 1,000 Births, 400 Gm. and Above	Perinatal Mortality per 1,000 Births, 1,000 Gm. and Above	State Average, 400 Gm. and Above	Rank Among Hospitals in State
1952*	7	...	...	...	...
1953	362	55.24	38.67	38.7	144
1954	516	53.47	46.51	37.4	138
1955	556	48.56	41.36	38.2	127
1956	603	44.77	28.19	37.5	89
1957	684	38.01	23.39	...	...
Total	2,728	48.75	34.45		

* 3 deaths in immature infants.

Table 2 gives the causes of death of immature infants and those weighing 1,000 Gm. and above. The classification of the causes of death is similar to that used by Anderson and Nesbitt at the Johns Hopkins Hospital [2] and that used by Potter at the Chicago Lying-in Hospital.[3] The principal difference between the classifications is the emphasis placed on premature rupture of the membranes. Infants whose deaths were due solely to premature labor being initiated by premature rupture of the membranes were assigned to this group rather than to that of abnormal pulmonary ventilation or infection.

Causes of Death in Premature and Mature Infants.—The principal cause of death in premature and mature infants was anoxia. Thirteen and nine-tenths per cent of the deaths were due to premature separation of the placenta and rupture of the marginal sinus; 4.3% were due to prolapse or compression of the umbilical cord; and 3.2% of the infants died as a result of placenta previa. These major obstetric problems accounted for 21.4% of the total deaths. The second most important cause, toxemia of pregnancy, accounted for 16.1% of the deaths. Since a reduction in fetal oxygenation is also the principal cause of death in infants whose mothers have toxemia of pregnancy, anoxia was thought to be the cause of death in 37.5% of these infants. Other significant causes of death were premature rupture of the membranes and congenital malformations.

TABLE 2.—*Cause of Death of All Infants Delivered at North Carolina Memorial Hospital, 1952 to 1958*

	400-1,000 Gm.				1,000 Gm. and Above			
	Fetal Deaths, No.	Neonatal Deaths, No.	Perinatal Deaths Total No.	Perinatal Deaths %	Fetal Deaths, No.	Neonatal Deaths, No.	Perinatal Deaths Total No.	Perinatal Deaths %
Placenta previa	0	0	0	0	1	2	3	3.2
Premature separation of placenta or marginal sinus rupture	2	3	5	12.8	8	5	13	13.9
Prolapse or compression of cord	1	0	1	2.6	4	0	4	4.3
Maternal complications	0	1	1	2.6	3	0	3	3.2
Complications of labor	0	0	0	0	2	0	2	2.2
No abnormal state	1	1	2	5.1	5	3	8	8.6
Toxemia of pregnancy	6	0	6	15.4	13	2	15	16.1
Diabetes mellitus	0	0	0	0	6	0	6	6.5
Birth injury	0	3	3	7.7	3	0	3	3.2
Malformation	0	0	0	0	8	5	13	13.9
Erythroblastosis or ABO incompatability	0	0	0	0	3	1	4	4.3
Infection	0	0	0	0				
Syphilis	0	0	0	0	1	0	1	1.1
Other infection	0	1	1	2.6	1	3	4	4.3
Premature rupture of membranes	4	8	12	30.8	9	4	13	13.9
Abnormal pulmonary ventilation	0	8	8	20.5	0	2	2	2.2
Total	14	25	39	100.0	67	27	94	100.0

perinatal mortality rate. There has been an increase in the resident staff as well as in the awareness of the importance of reducing perinatal mortality and morbidity on the obstetric and pediatric services.

The reduction in perinatal mortality has resulted in an improvement in the relative rank of the North Carolina Memorial Hospital among other hospitals in the state. It is evident, however, that the fetal and neonatal mortality in a teaching institution which accepts indigent nonwhite as well as white patients cannot be realistically compared with a hospital which accepts only white private patients. Perinatal mortality does not necessarily reflect the quality of the obstetric care; it may also reflect the socioeconomic level of the patients delivered. This is just as true in New York City as it is in North Carolina.[1]

Causes of Death in Immature Infants.—The principal cause of death in immature infants was premature rupture of the membranes. Premature rupture of membranes has generally not been listed as an important item in perinatal mortality. A recent study in the three teaching institutions in North Carolina indicated that 15.8% of all deliveries were complicated by this condition while 26.7% of all perinatal deaths were associated with premature rupture of membranes.[4] Believing this complication to be of significance, preference was given to it when there were no other obvious causes of death. Toxemia of pregnancy was an important factor in the deaths of 15.4% of these small infants. Premature separation of the placenta as well as rupture of the marginal sinus accounted for 12.8% of the deaths. Birth injuries, generally associated with anoxia, accounted for 7.7% of these deaths in immature infants.

Socioeconomic Aspects

Recent studies have indicated the importance of parental, fetal, and environmental factors in perinatal mortality.[5] These same factors were found to be important in this material.

Table 3 shows the perinatal mortality in the North Carolina Memorial Hospital according to race and admission status. The perinatal mortality of all deliveries was 48.8 per 1,000 births; for premature and mature infants it was 34.5. When one compares the mortality among the staff patients with that in private patients and similarly for nonwhite and white patients, it is evident that the majority of the deaths were among staff and nonwhite infants. This is even more apparent when the perinatal mortality for the nonregistered group is reviewed. The nonregistered patients were generally indigent white and nonwhite mothers referred from rural hospitals and clinics. The mortality of these immature unregistered infants was 294.9 per 1,000 births, while the death rate for the premature and mature infants was 160.3. When the unregistered group is eliminated from the data, the perinatal mortality in the registered staff and private group approaches a reasonable and acceptable rate of 27.2 and 23.3, respectively, per 1,000 births.

TABLE 3.—*Perinatal Mortality at North Carolina Memorial Hospital According to Race and Admission Status*

Status	Deliveries, No.	Perinatal Mortality per 1,000 Births: 400 Gm. and Above (Total)	Perinatal Mortality per 1,000 Births: 1,000 Gm. and Above
All deliveries	2,728	48.75	34.45
Staff deliveries	1,737	61.02	39.14
Private deliveries	991	27.24	26.23
White	1,816	33.31	27.53
Nonwhite	912	77.85	48.24
Nonregistered*	156	294.87	160.25
Staff-registered	1,581	37.95	27.19
Private-registered	987	23.27	23.27
Total registered	2,568	32.32	25.70
Total	2,728	48.75	34.45

* No prenatal care at North Carolina Memorial Hospital.

There is a striking contrast between the causes of death in private patients and unregistered patients. Malformations accounted for 25.9% of the infant deaths among private patients, while there were no deaths from this cause among nonregistered patients. Toxemia of pregnancy was the principal cause of death in 7.4% of the private patients but 37.5% and 27.3% of the nonregistered group. Premature rupture of membranes did not contribute to a single death in the private patient group, but it was a major factor in the death of 8.3% of the premature and mature infants and 27.3% of the immature infants among nonregistered patients. When major obstetric complications do not occur in a group of patients, there will be an increase in the percentage of nonpreventable causes of death, such as congenital malformations and erythroblastosis.

TABLE 4.—*Cause of Death Among Private and Unregistered* Patients Delivered at North Carolina Memorial Hospital, 1952-1958*

Cause of Death	All Private Patients: No.	All Private Patients: %	Unregistered Patients: 1,000 Gm. and Above: No.	Unregistered Patients: 1,000 Gm. and Above: %	Unregistered Patients: Under 1,000 Gm.: No.	Unregistered Patients: Under 1,000 Gm.: %
Placenta previa	3	11.1	0	0	0	0
Premature separation of placenta or marginal sinus rupture	4	14.8	4	16.7	2	9.1
Prolapse or compression of umbilical cord	1	3.7	0	0	1	4.5
Maternal complications	1†	3.7	2	8.3	1	4.5
Complications of labor	0	0	1	4.2	0	0
No abnormal state	4	14.8	1	4.2	0	0
Toxemia of pregnancy	2	7.4	9	37.5	6	27.3
Diabetes mellitus	1	3.7	3	12.5	0	0
Birth injury	1	3.7	0	0	1	4.5
Malformations	7	25.9	0	0	0	0
Erythroblastosis or ABO incompatability	3	11.1	0	0	0	0
Infection	0	0	2	8.3	1	4.5
Premature rupture of membranes	0	0	2	8.3	6	27.3
Abnormal pulmonary ventilation	0	0	0	0	4	18.2
Total	27	100.0	24	100.0	22	100.0

* No prenatal care at North Carolina Memorial Hospital.
† Poliomyelitis.

Table 4 compares causes of death in the private and unregistered groups. Perinatal mortality due to premature rupture of membranes is clearly a complication among nonwhite staff patients; it was associated with 25.6% of the perinatal deaths. When premature rupture of membranes occurs among infants weighing over 2,000 Gm. (4½ lb.) in the white private patients, it is of minor importance; but when this complication occurs in lower socioeconomic groups, both white and nonwhite, it is a particularly lethal complication.[4]

Table 5 shows data on toxemia of pregnancy and premature separation of the placenta and rupture of the marginal sinus in regard to status of the pa-

tient. Toxemia of pregnancy is also seen to be a complication among nonwhite staff patients. Thirty per cent of all deliveries on the obstetric service are nonwhite, but 70% of the cases of toxemia of pregnancy occurred in this group. Moreover, 93.3% of the cases of toxemia occurred among staff patients, but only 6.7% of the cases occurred among private patients. It is important to note that 22.6% of all of the infant deaths were associated with toxemia of pregnancy.

Premature separation of the placenta and rupture of the marginal sinus also were related to the socioeconomic status of patients. Of the total of these hemorrhagic complications, 55.6% occurred in nonwhite mothers, while only 30% of the deliveries were in this group. Of the total cases of premature separation of the placenta or marginal sinus rupture, 77.8% occurred in staff patients, while 22.2% occurred in private patients. Of all the perinatal deaths, 13.5% were associated with this complication.

TABLE 5.—*Analysis of Premature Rupture of Membranes and Toxemia of Pregnancy as Causes of Perinatal Deaths*

	Premature Rupture of Membranes*		Toxemia of Pregnancy†	
	No.	%	No.	%
Race and admission status				
Nonwhite	22	64.7	21	70.0
White	12	35.3	9	30.0
Staff	31	91.2	28	93.3
Private	3	8.8	2	6.7
Registered	26	76.5	11	36.7
Unregistered	8	23.5	19	63.3
Birth weights, Gm.				
400 to 999	16	47.2	6	20.0
1,000 to 2,499	13	38.2	14	46.7
2,500 and above	7	20.6	10	33.3
Importance as cause of death				
Primary	20	58.8	20	66.7
Contributing	8	23.5	5	16.7
Miscellaneous factors				
Associated with premature separation of placenta	5	14.7	3	10.0
Febrile (above 99 F)	12	35.3	7‡	23.3‡
Not febrile	22	64.7	..	...

* 25.6% of all with premature rupture of membranes.
† 22.6% of all deaths were associated with toxemia of pregnancy.
‡ Associated with fetal distress.

A previous review [5a] of the material in the North Carolina perinatal mortality study revealed that the father's occupation and the mother's education were probably of major importance in fetal and neonatal deaths. The death rates per 1,000 single births of infants weighing 400 Gm. and above, according to three occupation groups of the fathers, are as follows: group 1 (professional people, managers, officials, proprietors, and university students), 29.5 for white infants; group 2 (clerks, sales workers, craftsmen, foremen, and operators), 53.6 for white infants and 46.2 for nonwhite; and group 3 (farmers, farm laborers, other laborers, and household workers), 111.8 for white infants and 82.2 for nonwhite. It is clearly evident that the father's occupation is significant in its relationship to perinatal mortality. Figures for white and nonwhite persons should not be compared, since the occupations of many of the nonwhite fathers were not known and therefore could not be used in the tabulations.

The perinatal deaths, per 1,000 births, in relation to the education of the mother are as follows: among those with more than 12 years of education, 28.0 for white infants; 9-12 years, 65.7 for white infants and 48.9 for nonwhite; and 8 years or less, 70.5 for nonwhite infants. There were insufficient cases for an analysis of nonwhite mothers with more than 12 years of education and white mothers with 8 or less years, but the data available show a distinct correlation with the mother's education and perinatal mortality.

Incidence of Cesarean Section

Eastman [6] has indicated that the incidence of cesarean section in maternity hospitals is between 2 and 6%. There are, however, some private hospitals with a cesarean section rate of over 10%.

The incidence of cesarean section in the North Carolina Memorial Hospital for the five-year period, for a total of 2,700 deliveries, was 58, or 2.15%. However, the incidence among 1,717 staff patients was 27, or 1.57%, and the rate for 983 private patients was 31, or 3.15%. A review of each perinatal death indicated that a more conservative attitude was taken concerning cesarean sections among staff patients than among private patients. There were nine possibly indicated but not performed sections among staff patients but only one section which was possibly indicated but not performed among private patients. Had these 10 patients had abdominal deliveries, the incidence of cesarean section for the service would have been 2.52% and the incidence among staff and private patients would have been 2.09% and 3.25% respectively.

The section rate among staff and private patients should be about equal, with the incidence of the operation being slightly higher among staff patients. It is important to audit at periodic intervals the cesarean sections done on a service so that the incidence of the operation among private patients does not become too high while the incidence of the operation among staff patients does not remain too low.

Possible Errors in Obstetric Management

It is sometimes difficult but always important to analyze all perinatal deaths for possible errors in obstetric and pediatric management. There were 133 perinatal deaths among the 2,728 deliveries between 1952 and 1958. There were 12 deaths (9%) where the obstetric management of the patients while they were in the North Carolina Memorial Hospital possibly could have been improved.

Fetal Distress.—There were five cases of error in the management of fetal distress. Cesarean section probably should have been performed in four of these. Induction was not done in the case of a postmature infant with premature rupture of membranes and the passage of meconium. Concealed hemorrhage was not promptly diagnosed and treated. There was a delay in the diagnosis and treatment of a patient with prolapse of the umbilical cord. Oxytocin (Pitocin) stimulation was continued despite a persistent bradycardia (100 to 110 per minute) in a patient with severe toxemia of pregnancy. Another patient was not properly observed during oxytocin stimulation.

Toxemia of Pregnancy.—The principal errors in the management of patients with toxemia of pregnancy were due to the failure to realize the importance of albuminuria and a reduction in fetal growth. One patient, with severe toxemia, had fetal death in utero when there was an inordinate delay in induction. A second patient had persistent albuminuria and failure of the uterus to increase in size over a four-week period. Fetal death in utero occurred before induction was attempted. A third patient was not promptly admitted to the hospital when severe toxemia developed.

Diabetes.—The major causes of perinatal deaths in pregnant diabetic women in the North Carolina Memorial Hospital has been a failure of referring physicians to provide proper prenatal care and a failure of the patients to cooperate in the obstetric and medical management of their diabetes. There was no correlation between the perinatal mortality among pregnant diabetic women in this hospital and White's classification of such patients [7]; the death rates were a function of the intelligence and socioeconomic status of the mother. Cesarean sections, however, should probably have been done on two patients with excessively large infants, one patient with an abnormal presentation, and one patient with uterine inertia.

Anesthesia and Analgesia.—It is difficult to assess the role of anesthesia and analgesia in perinatal mortality because of the multiplicity of factors that are so often present in an infant's death. However, each death was carefully reviewed as regards to the role played by anesthetic and analgesic agents. It was felt that there were no deaths in mature infants which were related to analgesic or anesthetic drugs. In 25 of the 45 premature infants who died in the neonatal period, however, mothers received at least one analgesic or anesthetic agent during labor. It is felt that this is not consistent with the best obstetric practice. In general, premature infants have the best chance of survival when no analgesia or anesthesia is used and delivery is conducted with the patient under a pudendal block and with administration of 100% oxygen.

Neonatal Deaths

The autopsy material and clinical records of the 63 neonatal deaths were reviewed in order to determine the causes of death of these infants. The major problems of the neonatal period were prematurity in 26 cases, birth injury in 13, and infection in 9. These and other factors in neonatal deaths are summarized in table 6.

Summary and Conclusions

A study of the perinatal mortality in 2,728 deliveries conducted in the North Carolina Memorial Hospital showed the principal causes of death to be hemorrhagic complications, toxemia of pregnancy, congenital malformations, and premature rupture of the membranes. It is felt that premature rupture of the membranes should receive increased attention as an important cause of perinatal mortality. There was a significant correlation between the socioeconomic status of the patients and perinatal mortality. The highest perinatal mortality occurred among the lower socioeconomic group of patients, whether the classification was based on the mother's education, on race, or on the father's occupation.

The principal errors in obstetric practice were related to the management of fetal distress, toxemia of pregnancy, and diabetes. A reduction in perinatal mortality can occur with improved obstetric care. This reduction will be most significant when it is associated with an improvement in

TABLE 6.—*Autopsy Findings or Clinical Diagnoses in Sixty-three Cases of Neonatal Deaths at North Carolina Memorial Hospital, 1952-1958*

	Total
Prematurity	26(41.1%)
Alone	9
With atelectasis	15
With ventricular hemorrhage	1
With adrenal hemorrhage	1
Postnatal asphyxia and atelectasis	3(4.8%)
Atelectasis alone	1
Hyaline membrane	2
Infection	9(14.3%)
Pneumonia with maternal sepsis	3
Pneumonia, cause unknown	2
Septicemia with maternal sepsis	1
Meningitis with traumatic delivery	1
Enterocolitis and pneumonia	1
Sudden death with tracheitis	1
Congenital malformations	8(12.7%)
Multiple, severe	2
Congenital diaphragmatic hernia	2
Polycystic liver and kidneys	1
Nephroblastoma and polydactyly	1
Esophageal atresia	1
Ileal atresia	1
Birth injury	13(20.7%)
Subarachnoid or subdural hemorrhage*	12
Traumatic delivery	1
Erythroblastosis	2(3.2%)
Fetal hydrops	1
Severe early jaundice and kernicterus	1
Sudden death with no significant findings	1(1.6%)
Unknown	1(1.6%)

* 11 in premature infants.

the socioeconomic status of the obstetric patients and a reduction in the birth rate among indigent mothers.

North Carolina Memorial Hospital.

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UROLOGIC PROBLEMS IN REHABILITATION OF HEMIPLEGIC PATIENTS

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The records of 254 patients with hemiplegia resulting from cerebral vascular accidents have been studied for evidence of an association between urinary incontinence and ability to regain ambulatory status. The patient who has had a stroke must be watched for evidence of urinary dysfunction, especially since incontinence may be evidence of retention. Its persistence is not always due to impairment of cortical control; it may be the result of coincident urologic disease. The data from this study showed that persistent urinary incontinence was associated with delay or failure of the recovery process with respect to ambulation, but the causal relation was complicated. The functions of ambulation and urination are both impaired by the loss of cortical control, but incontinence also causes difficulties in transportation and in rehabilitative procedures. The control of incontinence by the various measures suggested here is an important step in the rehabilitative process.

In a previous investigation[1] into the causes for failure to achieve independent ambulation in a group of hemiplegic patients, we noted that a high proportion of the patients with failures had associated urinary incontinence. Our purpose, therefore, has been to see if incontinence played a significant role as a cause for failure to achieve independent ambulation and to study the relationship of incontinence to other factors which are present, such as the mental status, emotional status, positive motivation for independence, severity of the muscular involvement, and aphasia. We were interested in the effects of the central nervous system lesions as well as in the possibility of local pathology within the genitourinary tract as further complicating problems. Some of these local pathological problems were preexistent to the hemiplegia, and others developed as complications of the stroke. In the past, it has been generally felt that persistence of incontinence is a poor prognostic sign for independence. We were interested in seeing if this were true on the basis of our own cases and in determining if there

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were other correlations which might be of value in prognosis as to recovery of bladder control and achievement of independent ambulation.

Method

We have reviewed the records of 254 consecutive inpatients admitted to the rehabilitation service of the Burke Foundation with the diagnosis of cerebral vascular accident resulting in hemiplegia. Patients were unselected and were not screened prior to admission. The cases were previously classified at time of discharge only in terms of ambulation as (1) success (completely independent with or without cane or brace), (2) premature discharge (insufficient time for recovery or therapy), (3) unfeasible for rehabilitation (general medical or mental condition unsatisfactory), (4) deteriorated (became acutely ill and therapy discontinued), or (5) failure. The failures, in terms of completely independent ambulation, were classified as "true failures" (TF) if ambulation was safely limited to parallel bars even with maximum support by a therapist, "assistance" (A) if patient required minimal assistance to give support or balance outside of parallel bars, or "observation" (OBS) if patient required observation outside the parallel bars to provide occasional assistance for balance and support. Patients in groups A and OBS generally could be expected to walk satisfactorily about the ward or home with an attendant or relative and thus are failures only in the sense of our definition of terms, the condition actually having improved significantly. Many in groups A and OBS also would be expected to continue to improve after discharge and ultimately arrive in our success group.

All patients who manifested urologic problems were analyzed as to success and failure in ambulation, diagnosis of urologic problems, age, sex, presence or absence of organic mental syndrome, emotional state, site of lesion, bilateral or multiple involvement, associated illness, recovery of urologic problems, and aphasia.

Physiology of Micturition

The bladder is controlled by two reflex mechanisms: 1. The spinal (cord) mechanism consists of an afferent and efferent limb synapsing in the sacral cord. Filling of the bladder is an adequate stimulus for this arc. When a sufficient threshold is reached the motor impulse is carried over the efferent limb resulting in contraction of the bladder detrusor urinae. 2. The suprasegmental (cortex, midbrain, and hindbrain) mechanism consists of afferent and efferent pathways between the brain and the cord. The afferent pathways carry the impulses of bladder sensation to consciousness, while the efferent pathways carry tonically active subconscious inhibitory impulses which prevent involuntary contraction of the bladder in adults and maintain sphincter tone.

Micturition results from a stretch reflex (spinal reflex) or the reaction by contraction of muscle fibers to the stimulus of stretching. The reflex center is in the sacral portion of the spinal cord. Impulses from the distending bladder wall constantly reach the reflex center, but stimulation of the efferent (motor) parasympathetic neurons to cause detrusor contraction is inhibited by impulses from centers in the brain or brain stem. This activity remains below the level of consciousness until vesical distention or intravesical pressure reaches a critical level, at which point the individual becomes aware of a desire to void. If the time and place are not propitious, inhibiting impulses may be sent voluntarily down to the sacral cord to postpone micturition. When desired, these impulses are suppressed and the detrusor muscle allowed to contract in response to the stretch reflex. Voiding is facilitated by contraction of the abdominal muscles and lowering of the diaphragm. The vesical neck gradually opens, the external sphincter opens abruptly, and voiding takes place. Contraction of the detrusor muscle is maintained until all of the urine is evacuated, and this is believed to be a manifestation of cerebral control.

TABLE 1.—*Types of Urologic Problems in Hemiplegic Patients During Rehabilitation*

Group	Patients, No.		Condition	Manifestation
	Men	Women		
Ambulatory	4	5	Loss of cortical inhibition	Incontinence of bowel and bladder
	3	1	Loss of cortical inhibition	Nocturnal incontinence
	1	...	Benign prostatic hypertrophy-prostatitis	Hematuria
	...	3	Cicatricial urethritis	Retention and incontinence
Nonambulatory	19	18	Loss of cortical inhibition	Incontinence of bowel and bladder
	1	...	Loss of cortical inhibition and postoperative carcinoma of prostate	Incontinence of bowel and bladder
	...	6	Loss of cortical inhibition and cicatricial urethritis	Incontinence of bowel and bladder and retention
	3	2	Loss of cortical inhibition	Nocturnal incontinence
	3	1	Loss of cortical inhibition	Urinary incontinence
	2	...	Benign prostatic hypertrophy	Frequency
	2	...	Vesical neck obstruction with benign prostatic hypertrophy	Slight retention and frequency
	1	...	Vesical neck obstruction with benign prostatic hypertrophy	Complete retention
	...	1	Postoperative retention	Frequency; dysuria
	...	7	Cicatricial urethritis	Retention and incontinence

Results

In our group of 254 hemiplegic patients, 138 achieved independent ambulation prior to discharge. This is the success group. One hundred sixteen patients did not achieve independent ambulation; 64 of these were in the failure group, due to the neuromuscular status, and 52 were considered to be in the unfeasible, deteriorated, or premature discharge groups. Of the total group of hemiplegic

patients, 83 (32%) (table 1) were found to have had urologic problems during their period of rehabilitation. Of these, 17 were in the success group and 66 in the failure and unfeasible group.

The 17 patients in the success group who had urinary problems included 13 with lack of cortical inhibition, manifested in 9 by incontinence of bowel and bladder and in 4 by incontinence of bladder at night. This group consisted of 6 females and 7 males, and at the time of discharge 10 had become continent, 1 had improved, and only 2 remained incontinent of urine at night. The sex distribution of patients does not appear to be significant. There were 13 instances, however, of patients who manifested various degrees of organic mental syndrome and 8 instances of emotional disturbances which tended to clear up with improvement in control. Multiple strokes occurred in only one patient. Vesical neck obstruction occurred in three female patients in whom a diagnosis of cicatricial urethritis had been made. Manifestations included

TABLE 2.—*Characteristics of Continent and Incontinent Patients*

Group	Total	Hemiplegia		Organic Mental Syndrome	Emotional Disturbance	Bilateral Involvement	Multiple Involvement	Aphasia
		Right-Sided	Left-Sided					
Continent, successful rehabilitation								
Male	76	38	38	10	41	3	6	31
Female ..	45	17	28	3	22	2	6	14
Continent, unsuccessful rehabilitation								
Male	23	9	14	5	14	1	4	6
Female ..	27	12	15	5	16	2	3	9
Incontinent, successful rehabilitation								
Male	8	2	6	6	3	..	..	1
Female ..	9	5	4	7	5	..	1	2
Incontinent, unsuccessful rehabilitation								
Male	31	13	18	26	13	6	6	11
Female ..	35	18	17	27	15	5	5	17

urinary retention, frequency, urgency, and incontinence, chiefly nocturnal. Two of these patients became continent and symptom free, and one improved after treatment. Benign prostatic hypertrophy occurred in one male patient and was manifested by gross hematuria which cleared spontaneously after a period of catheterization with an indwelling catheter. In neither the vesical neck obstruction cases or the benign prostatic hypertrophy case was an organic mental syndrome present.

The 66 patients in the failure group who had urinary problems included 52 with loss of cortical inhibition due to the cerebral vascular accident; this was manifested in 37 by incontinence of bowel and bladder, 4 by urinary incontinence—day and night, 5 by nocturnal urinary incontinence, and 6 by incontinence of bowel and bladder complicated by cicatricial urethritis.

Fourteen patients manifested primary urologic problems; seven females had frequency, urgency incontinence, and dysuria secondary to cicatricial urethritis, with retention of urine and cystitis. All of these patients became continent. Five males had retention with urgency incontinence and nocturnal incontinence with secondary retention and cystitis due to benign prostatic hypertrophy. One male initially showed bowel and bladder incontinence secondary to loss of cortical inhibition, but as this cleared he manifested a premorbid urinary incontinence which had been present after a prostatectomy for carcinoma with apparent sphincter injury. One female patient, who had undergone hamstring release, developed urinary retention postoperatively due to poor bladder emptying and developed a cystitis with urgency incontinence. After treatment she became continent.

There is no significant difference in the characteristics of incontinent males as compared to incontinent females in either the success or failure groups, with the exception that the males were slightly older. Males and females showed essentially the same incidence of right-sided and left-sided hemiplegia, aphasia, incidence of bilateral or multiple involvement, incidence of cardiovascular disease, emotional disturbances, and organic mental syndromes. There is no significant difference between the sexes in incidence of urologic problems in either the success or failure groups (table 2).

When we compare the success group with the failure group of incontinent persons, regardless of sex, there is no significant difference of incidence of right-sided and left-sided hemiplegia, organic mental deficits, or emotional disturbance, but there is an increased incidence of aphasia, second strokes, and bilateral involvement in the failure group as compared to the success group. It is felt the organic mental changes were more severe in the failures.

The outstanding fact noted is the much greater incidence of urologic problems in the failure group —66 cases out of 116, or 56%, as compared to 12% of the success group. This failure group is made up of those patients for whom rehabilitation is considered unfeasible and those patients who did not achieve independent ambulation by the time of discharge. Among the incontinent failures were 22 cases of multiple strokes or bilateral involvement. In the failure group of 31 patients with hemiplegia on the right, 28 had aphasia; in the successful group 3 cases of aphasia occurred in 7 patients. Thus, there was a higher incidence of aphasia in the failure group. Of the 67 incontinent failures, 53 showed organic mental changes, as did 13 of the 17 in the successful group. The primary cause was loss of cortical inhibition alone in 56 patients, with cicatricial urethritis in six and benign prostatic hypertrophy in one. Seven patients had cicatricial urethritis alone, and six had benign prostatic hypertrophy alone.

The continent patients, as compared to the incontinent, showed a majority of successes and a decreased incidence of organic mental changes, multiple strokes, and bilateral involvement. Aphasia

in all groups occurred in a majority of patients with hemiplegia on the right; it did not appear to be significantly higher among the incontinent patients as such but was slightly higher in the failure group of both the continent and incontinent patients.

Observations After Cerebral Vascular Accident

During the initial phase of a stroke, with or without loss of consciousness, as a result of the neurological lesion, there is an interruption in the normal pathway of afferent impulses from the bladder wall to the cerebrum and the efferent pathways which permit cortical inhibition of the reflex of micturition. The loss of cerebral inhibition over reflex bladder contractions results in frequency, urgency, and urgency incontinence (precipitate micturition), not unlike that in a patient with uninhibited neurogenic bladder.

Bilateral lesions of the motor cortex usually give rise to such characteristic disturbances as (*a*) inability to initiate micturition voluntarily, (*b*) inability to stop the stream, and (*c*) urgency, frequency, and urgency incontinence due to lack of cerebral inhibition. The bladder is overactive and hyperirritable. The external sphincter may become hypertonic or even spastic with resultant retention.[2] The more extensive the lesion the more likely that bilateral dysfunction may occur, at least temporarily, and thus the greater likelihood of impaired cortical inhibition.

Thus, to a certain limited extent the situation is similar to that which occurs in a spinal cord transection with the development of an automatic bladder. In hemiplegia, of course, the situation is not as marked and generally there is recovery, since only the tracts of one side of the brain are affected and usually only temporarily. The loss of cortical inhibition of micturition permits the detrusor to contract frequently and with little force, thus giving rise to incontinence with urination occurring frequently in small amounts day and night. Normally, as the bladder fills and distends, cortical inhibition prevents urination through the action of the external sphincter and through inhibition of these mild detrusor contractions. Secondarily, in this phase, there is also a tendency for the bladder not to empty completely, so that there is usually some degree of residual urine. At times, urinary retention may be marked, particularly if some form of obstruction of the vesical neck is already present, and acute urinary retention may occur.

Prostatism in men is frequent in the stroke age group and contributes to retention, as does chronic cicatricial urethritis in the female. Retention may occur while the patient is unconscious, but with return of consciousness continued marked retention is uncommon, except in those with associated obstruction. After the acute phase of the cerebral vascular accident catheterization or an indwelling catheter may be necessary for prevention of the incontinence due to the loss of cortical inhibition, or it may be necessary also to prevent urinary retention due to this condition, plus a premorbid tendency to vesical neck obstruction which increases the amount of urinary retention.

Normally, as the patient regains consciousness and improves, cortical inhibition returns and the patient will regain normal bladder function. In a certain number of patients with hemiplegia, however, urinary incontinence continues as a problem. This is due to several factors, as follows:

1. The neurological impairment of the pathways may be such as to prevent normal function of cortical inhibition.

2. Organic mental changes with clouding of the sensorium or loss of motivation for control may cause the patient not to respond to the sensory stimuli of bladder distention and permit reflex emptying without cortical inhibition.

3. Preexisting vesical neck obstruction (such as prostatic hypertrophy in the male and cicatricial urethritis in the female) may have caused symptoms prior to the cerebral vascular accident. In these situations there has been urinary retention which leads to early attainment of the bladder threshold and hence frequent voiding. If the retention is marked, the patient may quickly reach a level of bladder distention which he is not able to control even if cortical inhibition is intact. Some of these patients, however, with only moderate retention, plus some loss of cortical inhibition, will develop frequency and urgency incontinence.

4. Local infection of the urethra, bladder neck, or prostate secondary to long-term or short-term retention or previous catheterizations adds to the symptomatology of frequency and urgency which may lead to incontinence at night when loss of cortical inhibition is most marked, whether due to psychological factors or to inherent neurological interference in the pathway.

5. Immobilization in bed, use of bedpan in supine position, weakness of abdominal and diaphragmatic contraction, lack of effort in attempting micturition through relaxation of sphincter and use of accessory muscles, and poor and ineffective detrusor contractions contribute to incomplete bladder emptying resulting in retention with tendency to cystitis, frequency, and urgency incontinence.

Management

If acute retention occurs, catheterization should be done every 8 hours, and if voiding is not spontaneous within 24 hours, an indwelling catheter may be used. After the patient has been fully conscious for 5 to 19 days, the catheter should be removed. Retention is uncommon, but if over 90 cc. of residual urine persists, the catheter should be replaced until the urologic problem is resolved. In such cases, the catheter must be irrigated daily with a bacteriostatic solution, such as benzalkonium

(Zephiran) chloride (1:20,000), and changed weekly. When the patient is able, habit training and supervised timed voidings will develop control.

If incontinence is a problem, check for retention, and if it is over 90 cc., replace the catheter temporarily. If the residual is small, incontinence is on the basis of poor cortical inhibition, and the catheter may be replaced temporarily to await further neurological recovery. The general condition should make it possible to decide on the necessity for an indwelling catheter. If possible, unless retention with infection is present, use of the indwelling catheter should be avoided.

Loss of cortical inhibition manifests itself in most severe form by bowel and bladder incontinence. Bowel incontinence can usually be brought under control first, both on an active and on a passive basis. This is done by achieving a bowel regimen with daily daytime evacuation, with use of bedpan or commode with suppository or enema as needed.

Bladder continence is achieved by stressing urination every two to three hours, synchronized to the patient's spontaneous detrusor contractions during waking hours, with late evening catheterization to remove residual and minimize nocturnal incontinence. When no residual occurs catheterization can be discontinued.

Trials without the catheter should be repeated periodically until the patient can do without or until neurological recovery has reached its zenith. If recovery has been poor and the patient still has urologic difficulty, prolonged catheter drainage (if there is a high residual of urine) or other device for incontinence, such as a rubber urinal, may be necessary. If recovery has been good but urologic difficulty persists, treatment for any underlying or preexisting uropathology should be instituted. In men, transurethral prostatic resection may be needed in those with benign prostatic hypertrophy. In women, urethral dilatation and local therapy to the bladder and urethra (nitrofurazone [Furacin] urethral suppository or dilute silver nitrate) may be helpful in cicatricial urethritis.

Parasympathicolytic drugs (such as methantheline [Banthine] bromide) are of little value usually when incontinence results from lack of cortical control rather than muscular hyperactivity, but they may be of symptomatic value in frequency secondary to low-grade infection. In this case, primary attention should be on culture of organisms and appropriate antimicrobial agents.

In all cases, after catheter removal, begin a supervised habit training schedule of voiding every two to three hours, gradually lengthening the intervals as recovery permits. Continual reorientation, encouragement, explanation, diminution of embarrassment, and use of sitting position, diaphragm, and abdominal muscles in voiding are essential in achieving urinary continence during recovery from loss of cortical inhibition.

With indwelling catheters, irrigate four times daily with sterile saline solution, boric acid, phosphoric acid, or half-strength G (Suby) solution. Also use ammonium chloride or methenamine mandelate (Mandelamine) to keep the urine acid. Change the catheter weekly, under sterile conditions. Intermittent prophylactic chemotherapy (full therapeutic dose for one week for each month) may be useful in lessening urinary tract infection.

Conclusions

The overwhelming cause of urinary incontinence was found to be loss of cortical inhibition, and urologic complications were usually secondary to this phenomenon. Frequency and dysuria frequently occurred as the result of preexisting vesical neck obstructive disease and or infection. Recovery from loss of cortical inhibition usually followed in the following phases: bowel and bladder incontinence, bladder incontinence, nocturnal urinary incontinence, and normal bladder control.

The high incidence of incontinence among those hemiplegics who failed to achieve independent ambulation was noted in a prior study when the causes of failure to achieve independent ambulation were being evaluated. Despite the high incidence it is not felt to be a causative factor in itself.

Persistence of urinary incontinence is a poor prognostic sign, but it must be evaluated in terms of all other factors present. A few patients remained incontinent when they became ambulatory. In none of our patients was this considered the reason for failure to achieve independent ambulation by itself but it usually indicated organic mental changes, poor motivation, emotional problems, and/or severe neuromuscular involvement. In most situations where independent ambulation was not achieved, the patient had not only bladder incontinence but also bowel incontinence.

Incontinence has been found to retard and impede achievement of independent ambulation because it causes difficulties in transportation and management of the patient in various clinics and gymnasiums and diminishes the enthusiasm and positive motivation of both the patient and the therapeutic team. Most instances of incontinence can be improved to the point of no interference with the rehabilitation treatment program through a habit-forming bladder program, positioning, encouragement, assistive abdominal and diaphragmatic contractions to achieve full bladder emptying, continued efforts at progressive physical activity and ambulation, a bowel training program with achievement of fecal continence, and the correction of local pathological situations in the urinary tract.

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D-PANTOTHENYL ALCOHOL IN MANAGEMENT OF PARALYTIC ILEUS

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The effectiveness of D-pantothenyl alcohol in the treatment of paralytic ileus was tested by comparing two groups of 50 patients after abdominal operations. Both groups received the customary postoperative care as seemed indicated by the attending surgeon, but in addition 50 patients received intramuscular injections of 250 mg. of D-pantothenyl alcohol every six hours until normal peristalsis was established, while the remaining 50 received a placebo in the same manner. In the group receiving the drug it was possible to discontinue the use of tubes and of venoclysis sooner than in the other group, but it was debatable whether the actual difference in the average case was of practical importance. The drug was used in 12 additional patients who had profound postoperative intestinal atony, and in each case it appeared to cause resumption of bowel sounds, passage of flatus, and relief from distention. No undesired side-effects were observed.

One of the distressing complications encountered after a surgical operation is adynamic ileus. Temporary paralysis of the intestine can result from direct injury to the intestine, chemical irritation, infection, reflex reaction to injury, and metabolic imbalances such as uremia and electrolyte deficiencies. Because of the serious consequences that may result from this complication, most surgeons today give considerable attention to its prevention. Modern practices of restoring good nutrition and blood volume before surgery, correction of electrolyte deficits, intestinal intubation, antibiotic preparation of the intestine, early ambulation, and other aids have helped in minimizing this syndrome.

Despite the infrequency of severe ileus, lesser degrees of intestinal paralysis are common. After any intra-abdominal procedure with its inherent trauma to the intestinal tract, a period of intestinal atony with mild distention may be expected. After this, many patients may have "gas pains" which usually herald the onset of intestinal peristalsis. The majority of patients then eliminate flatus and progress without incident to recovery of normal intestinal activity. For reasons that are not always clear, some patients have a delayed onset of peristalsis. They become distended and uncomfortable, necessitating the use of gastric suction, the rectal tube, enemas, and parasympathomimetic drugs. Most patients respond to these measures, but they are often physically exhausted by the regimen. Only the rare case is refractory and proceeds to true adynamic ileus. Any agent which would safely shorten the period of postoperative intestinal atony might decrease the discomfort due to the resumption of peristalsis and also be of value in the treatment of paralytic ileus. This study is an evaluation of an agent which may be useful in the prevention and treatment of paralytic ileus.

Review of Literature

D-Pantothenyl alcohol (Panthenol) is the alcohol of pantothenic acid, a vitamin of the B group. This vitamin, although included in most multi-vitamin preparations, has never been shown to be essential to human nutrition. It has been given to both animals and humans in very large doses with no toxic effects. Pantothenic acid is found in virtually every food eaten by man.

Early animal experiments demonstrated several interesting manifestations of pantothenic acid deficiency. McKibbin and co-workers [1] in 1940 described a deficiency syndrome in the dog which suggested to them a disorder of the parasympathetic nervous system. Bly and co-workers,[2] in 1943, using pantothenic acid-deficient dogs with jejunostomies, demonstrated a 50% decrease in intestinal motility and a 40% to 60% decrease in the absorption of carbohydrate and protein. Rats were fed a diet deficient in pantothenic acid by Jurgens and Pfaltz [3] in 1944 with the interesting finding of gas-filled atonic small intestines. This was alleviated rapidly by feeding pantothenic acid.

This latter study led Jacques [4] to use this vitamin in the treatment of adynamic ileus. He reported 16 severe cases with fecal vomiting that had not responded to all known therapeutic measures. Each patient was given 50 mg. of calcium pantothenate intramuscularly every three hours with uniformly good results. The passage of flatus, which Jacques considered the best sign of improvement, began 1½ to 13 hours after the initial injection. Banerji,[5] after reading Jacques' report, treated 19 patients with calcium pantothenate, with excellent results in 18. Favorable results in treating ileus with pantothenic acid were also reported by Zutelman,[6]

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Hofmann,[7] and Docherty.[8] The only report from the United States was by Bergman,[9] who treated 44 cases of ileus with favorable results. Felten[10] gave D-pantothenyl alcohol to 50 patients with severe gas pains, constipation, and distention after operation. He found that the majority expelled flatus in a few hours with marked subjective relief.

The uniformly good results reported seem to indicate that pantothenic acid is effective in restoring normal intestinal activity. The mechanism by which it exerts its effect remains unknown. Whereas pantothenic acid itself is not essential to nutrition, the discovery by Lipmann[11] of coenzyme A, which is a derivative of pantothenic acid, revealed the basic importance of the pantothenyl complex in cellular physiology. Coenzyme A is involved in the aerobic utilization of glucose, the synthesis of fatty acids, sterols, and steroids, and the acetylation of choline. It is this latter function which may be responsible for the action of D-pantothenyl alcohol in the intestinal tract.

TABLE 1.—*Type of Operations Performed on Fifty Patients Treated with D-Pantothenyl and Fifty with Placebo*

Type of Surgery	Group 1, D-Pantothenyl: No. of Cases	Group 1, D-Pantothenyl: Av. Time to Pass Flatus, Hr.	Group 2, Placebo: No. of Cases	Group 2, Placebo: Av. Time to Pass Flatus, Hr.
Gastric	13	40	12	55
Laparotomy; intestine not involved	13	32	11	60
Biliary	9	34	8	63
Intestine resection and anastomosis	6	36	8	75
Intestinal obstruction	4	24	4	78
Peritonitis due to perforated viscus	3	36	4	91
Appendectomy	2	24	3	48
Total	50		50	

Materials and Methods

Group 1.—One hundred unselected patients undergoing various intra-abdominal surgical procedures were used as the primary group for this study. Each patient was prepared for surgery with the usual examinations and preliminary procedures. Identical multiple dose vials containing D-pantothenyl alcohol and a placebo were used. The identifying code was on a removable label. Material for treatment was supplied to the ward with only the patient's name, the code having been removed. A list of the patients and the agent used was recorded. The clinical observers were not aware of the nature of the drug being administered. Fifty patients received D-pantothenyl alcohol and 50 others the placebo. The initial dose was started in the recovery room immediately after each operation and was continued until normal peristalsis was restored. Dosage was standardized at 1 cc. or 250 mg. of the active D-pantothenyl alcohol every six hours intramuscularly; a similar volume of the placebo was administered.

Group 2.—A second group of 12 patients who developed varying degrees of postoperative intestinal atony were treated with 250 mg. of D-pantothenyl alcohol intramuscularly every six hours until normal peristalsis was established.

In a study of this type the most difficult aspect was the evaluation of subjective complaints in the face of the many variables inherent to the postoperative period. All patients were treated as seemed indicated by the attending surgeon. No measure was added or withheld from the patient because of this study. Intestinal tubes, enemas, and other aids were used as deemed necessary. As a measurable end-point indicating the desired effect of the drug, the time of onset of audible peristalsis and the time of passage of flatus were selected. These observations were usually made at 6-hour to 12-hour intervals.

Results

Group 1.—Of the 100 patients treated by the double blind control method, 50 patients received D-pantothenyl alcohol and 50 others the placebo. Comparison of these two groups reveals them to be similar in most significant clinical aspects, including age and sex. Since the factor most likely to affect intestinal motility in the postoperative period was the type and extent of the surgery performed, the similarity of both groups is compared in table 1. Such factors as the duration of the operative procedures, the type of anesthetic agent, and the general condition of the patient were recorded and found to be essentially similar in both groups.

The 50 patients receiving D-pantothenyl alcohol developed audible peristalsis in an average of 25 hours postoperatively as compared to 55 hours in the control group. The passage of flatus was noted at an average of 48 hours in contrast to 66 hours in the placebo group. Since the appearance of bowel sounds and the passage of flatus indicate a resumption of intestinal activity, the figures seem to reflect a shortening of the period of postoperative atony in the treated group. No patients in group 1 and six patients in the control group developed signs of early ileus in the late postoperative period.

Table 2 divides the patients in the treated and control groups into comparable age groups. The time required to pass flatus averaged at least 24 hours longer in the control group in each division. Age per se did not influence the period of postoperative atony in either group.

Since patients with intestinal surgery or peritonitis are most likely to develop intestinal atony, similar types of operative procedures are compared in table 1. Three patients with diffuse peritonitis due to perforated intestine were treated with D-pantothenyl alcohol with the passage of flatus in an average of 36 hours as compared to four patients in the control group with atony for an average of 91 hours. Resection of the intestine with anastomo-

sis was accomplished in six patients treated with D-pantothenyl alcohol with the average time for passing flatus of 36 hours as compared with eight patients in the placebo group who required 75 hours to achieve the same result. In each group were four patients with mechanical intestinal obstruction relieved by operation. The four treated with D-pantothenyl alcohol were expelling flatus in an average of 24 hours, whereas the controls averaged 78 hours. The onset of peristalsis in the control group was similarly prolonged after gastric surgery, biliary surgery, appendectomy, and laparotomies for lesions not involving the intestinal tract.

Of the 50 patients treated with D-pantothenyl alcohol, only 1 developed nausea and vomiting. This case seemed to be a failure of treatment until obstruction of the gastroenterostomy stoma was demonstrated. After the obstruction cleared the patient proceeded to complete and rapid recovery. One patient undergoing a right colectomy had no peristalsis for four days but then progressed normally. In each of the 50 cases, after normal peristalsis returned, the patients continued to complete recovery with no later intestinal dysfunction.

Of the 50 patients treated with the placebo, 6 developed a recurrence of abdominal distention and absent bowel sounds after the usual period of postoperative atony had cleared. In three of these, gastric suction was reinstituted along with multiple enemas with clearing of the ileus within 48 hours. D-Pantothenyl alcohol, 250 mg. every six hours, was given to the other three after the drug code was broken. Two of these passed large amounts of flatus within 12 hours while the third was free of distention 36 hours after institution of therapy.

In evaluation of the more subjective data it was found difficult to grade symptoms. All patients complained of discomfort in the early postoperative period, but the majority in both the treated and control groups had minimal complaints after the first 24 hours. Complaints most often registered included abdominal soreness and discomfort from intestinal tubes and intravenous therapy. Nausea and vomiting were unusual after the immediate postanesthetic period. It was noticed that, once normal peristalsis returned, the patient usually felt better even when there were no specific complaints. In the treated group the earlier resumption of intestinal function allowed the earlier elimination of tubes and intravenous administration of fluids and thus in effect gave a measure of indirect subjective relief.

Group 2.—Of the 12 selected patients treated with D-pantothenyl alcohol because of profound postoperative intestinal atony, in each case abdominal distention, absent bowel sounds on auscultation, and marked subjective complaints such as abdominal discomfort, nausea, and fulness were present. These cases are presented briefly.

CASE 1.—A 12-year-old girl with a ruptured appendix had an appendectomy. Twenty-four hours after operation, marked distention with absent peristaltic sounds had developed despite intestinal suction. D-Pantothenyl alcohol was given, with resumption of bowel sounds after 3 hours and the passage of flatus after 12 hours. All distention had cleared and the patient felt greatly improved within 24 hours.

CASE 2.—A 22-year-old woman with acute pelvic cellulitis underwent exploratory laparotomy. Twenty-four hours after operation, marked distention was present and peristalsis was absent. Nausea and vomiting were severe. D-Pantothenyl alcohol was given, with the passage of flatus in 3 hours and clearing of all distention within 24 hours.

CASE 3.—A 30-year-old woman with carcinoma of the cervix had radical hysterectomy and lymphadenectomy. Twenty-four hours after operation, distention and a silent abdomen were noted despite intestinal suction. D-Pantothenyl alcohol was given with bowel sounds and passage of flatus within 12 hours. Normal peristalsis and a flat abdomen were noted within 24 hours.

CASE 4.—A 34-year-old man fractured his ribs on the left side. Three days after injury marked distention, a silent abdomen, and considerable discomfort had developed. Enemas, gastric suction, and rectal tubes had not helped. D-Pantothenyl alcohol was given, with the passage of flatus and subjective relief within 12 hours. All distention cleared within 24 hours.

TABLE 2.—*Age Distribution of Fifty Unselected Patients Treated with D-Pantothenyl and Fifty with Placebo*

	Group 1, D-Pantothenyl		Group 2, Placebo	
Age, Yr.	No. of Cases	Time for Passage of Flatus, Hr.	No. of Cases	Time for Passage of Flatus, Hr.
0-20	3	48	2	108
20-40	13	33	14	57
40-60	22	35	20	72
60-80	12	40	13	67
80 or over	0	...	1	60
Total	50		50	

CASE 5.—A 25-year-old man with intestinal obstruction secondary to adhesions after gastrectomy had lysis of adhesions. Three days after relief of the obstruction, the abdomen became markedly distended with hypoactive bowel sounds. A recurrent obstruction was suspected. D-Pantothenyl alcohol was given, with resumption of active bowel sounds and passage of flatus within 12 hours. All distention cleared within 36 hours with complete subjective relief.

CASE 6.—An 89-year-old woman with obstruction of the large intestine underwent loop colostomy followed by right colectomy. On the ninth day after the colectomy, bowel sounds disappeared and the abdomen became markedly distended and silent. It was feared that reintubation would be necessary. D-Pantothenyl alcohol was given, with the return of bowel sounds within a few hours, and flatus with a large bowel movement within 12 hours.

CASE 7.—A 31-year-old woman had tubo-ovarian abscess with peritonitis and underwent salpingectomy. Thirty-six hours after operation, marked distention, nausea, vomiting, and absent bowel sounds were noted. D-Pantothenyl alcohol was given followed within 6 hours by the explosive passage of flatus with clearing of distention within 24 hours.

CASE 8.—A 52-year-old woman with intestinal obstruction due to adhesions had lysis of adhesions. On the fourth day after surgery, distention was marked, with a silent abdomen. A single dose of D-pantothenyl alcohol was given with the passage of flatus in three hours followed by a bowel movement that evening.

CASE 9.—A 41-year-old woman with pelvic inflammatory disease had a hysterectomy. On the seventh postoperative day the patient developed fever, a silent abdomen, and distention. D-Pantothenyl alcohol was given with the passage of flatus within 3 hours and clearing of the ileus within 24 hours, even though her fever persisted until an abscess was drained four days later.

CASE 10.—A 40-year-old woman with carcinoma of the cervix had radical hysterectomy and lymphadenectomy. Thirty-six hours after operation she developed marked distention, with a silent abdomen. D-Pantothenyl alcohol was given with the passage of flatus within a few hours. The patient felt better within 24 hours, but 48 hours were required for the distention to clear completely.

CASE 11.—A 25-year-old woman with cholelithiasis had cholecystectomy. On the second day after operation she became distended, with no bowel sounds. D-Pantothenyl alcohol was given, with resumption of peristalsis within 12 hours and the passage of flatus within 24 hours.

CASE 12.—A 66-year-old woman with carcinoma of the ovary underwent total hysterectomy. Twenty-four hours after operation, marked distention and absence of bowel sounds developed. D-Pantothenyl alcohol was given, with resumption of good bowel sounds and the passage of flatus within 24 hours. All distention cleared within 48 hours.

In each case, D-pantothenyl alcohol appeared to produce a significant effect, although it was recognized that at least some of these patients might have improved spontaneously as rapidly without the drug. Further studies are needed, but the above cases are considered to be conclusive enough to treat subsequent cases of postoperative atony with this agent.

Side-effects.—Side-effects from the administration of D-pantothenyl alcohol could not be demonstrated. There was no complaint of excessive abdominal cramps, tachycardia, and flushing as is so often noted with parasympathomimetic drugs. At no time could symptoms be elicited due to an overdosage of the drug. No evidence of sensitivity, such as a rash, unexplained fever, or angioneurotic edema, was seen.

Comment

The inherent difficulty in evaluating any drug on the basis of clinical observation was apparent during this study. This difficulty was magnified during the postoperative period when so many variables were present, each affecting the well-being of the patient. It was felt, however, that this study represented an adequately controlled clinical evaluation.

D-Pantothenyl alcohol given in the immediate postoperative period appears to facilitate the resumption of normal peristalsis after operative procedures within the abdomen. It is debatable whether the actual difference in the average case is one of practical significance. The over-all difference demonstrated would not necessarily warrant the routine use of this drug in unselected cases. On the other hand, in the control group there were six patients who developed signs of early ileus in the late postoperative period who might not have had this difficulty if D-pantothenyl alcohol had been administered routinely. The prophylactic use of D-pantothenyl alcohol might be indicated in that group of patients in whom the type and magnitude of intestinal surgery is conducive to the development of paralytic ileus.

D-Pantothenyl alcohol gave excellent results in the 12 patients in group 2 treated for moderately severe intestinal atony as well as in 3 patients who developed distention after receiving the placebo. These findings are in agreement with the experience of other investigators. It would seem that D-pantothenyl alcohol is definitely indicated in those patients who appear to be developing postoperative distention. Certainly those patients with fully developed atony or classic adynamic ileus should be given the benefit of D-pantothenyl alcohol therapy.

The use of this drug is made more attractive by its apparent lack of toxicity as demonstrated both in this study and in the experience of others. The complete absence of abdominal cramps with tachycardia and flushing so often noted after the administration of a parasympathomimetic drug was striking. The most likely theory as to the reason for its effectiveness is that it stimulates the formation of acetylcholine through the coenzyme for acetylation (coenzyme A) of which pantothenic acid is a component. Thus the mode of action is through the "normal mechanism" controlling intestinal activity. The hesitation of many surgeons to use prostigmine-like drugs is often due to the fear that violent peristalsis might do damage to the operative site. D-Pantothenyl alcohol appears to be a safe yet effective agent capable of stimulating peristalsis and preventing paralytic ileus.

Summary and Conclusions

D-Pantothenyl alcohol and a placebo were administered alternately to 100 unselected patients undergoing intra-abdominal surgical procedures, utilizing the double blind control method. D-Pantothenyl alcohol appeared to shorten the duration of postoperative intestinal atony. Twelve other patients with moderately severe paralytic ileus were treated with D-pantothenyl alcohol. Within 24 hours, all 12 patients had resumption of peristalic activity as indicated by audible peristaltic sounds, the passage of flatus, and marked subjective relief. All distention had cleared within 48 hours. D-Pantothenyl alcohol appears to be a safe yet effective agent capable of stimulating peristalsis and preventing paralytic ileus.

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DISCOVERY OF TYPHOID CARRIER BY SEWAGE SAMPLING

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A method was applied for the bacteriological sampling of sewage through manholes at crucial points in an urban sewerage system in order to locate carriers of typhoid. The map shown here gives the arrangement of sewers in a city of 2,200 population where four cases had occurred in five years. The sampling method narrowed the field of inquiry to a small area, and bacteriophage typing of the Salmonella obtained yielded the final clue that led to identification of the carrier. The most significant advantage of this method is the ability to locate a carrier by use of a practical field study technique when the usual epidemiologic methods have failed.

In 1948, 1950, and 1952 Moore and his associates [1] reported the successful finding of typhoid and paratyphoid carriers by the continuous sampling of sewage for the presence of Salmonella. In their method, they suspended gauze strips (referred to as swabs) in the sewage flow and periodically removed and cultured them for Salmonella. Beginning at major sewage collection points, such as sewage treatment plants, they followed, as a consequence of positive findings, the source of organisms through lateral sewers to the homes of the carriers. Similar studies have been reported by a number of other investigators.[2] This sewage sampling procedure represents a new approach to the problem of locating carriers of enteric and other diseases in which the causative agent is present in the excreta. It also provides the epidemiologist with what appears to be an extremely valuable methodological tool.

Epidemiologic searches for carriers of enteric disease traditionally have followed a pattern of contact interviewing and analysis of the blood and excreta of suspected individuals. This method, although generally effective, has several drawbacks: 1. It may require a large number of trained field and laboratory workers. 2. Large numbers of specimens frequently must be obtained and processed before a positive finding is made. 3. People in the community are annoyed and sometimes alarmed by this type of investigation. Some individuals, especially those who have reason to believe that they themselves may be carriers, often refuse to cooperate. 4. A not unusual situation is the inability to locate the carrier by traditional epidemiologic methods in spite of repeated outbreaks of typhoid.

For some time the California State Department of Public Health has been interested in the swab technique. An opportunity to study and utilize the

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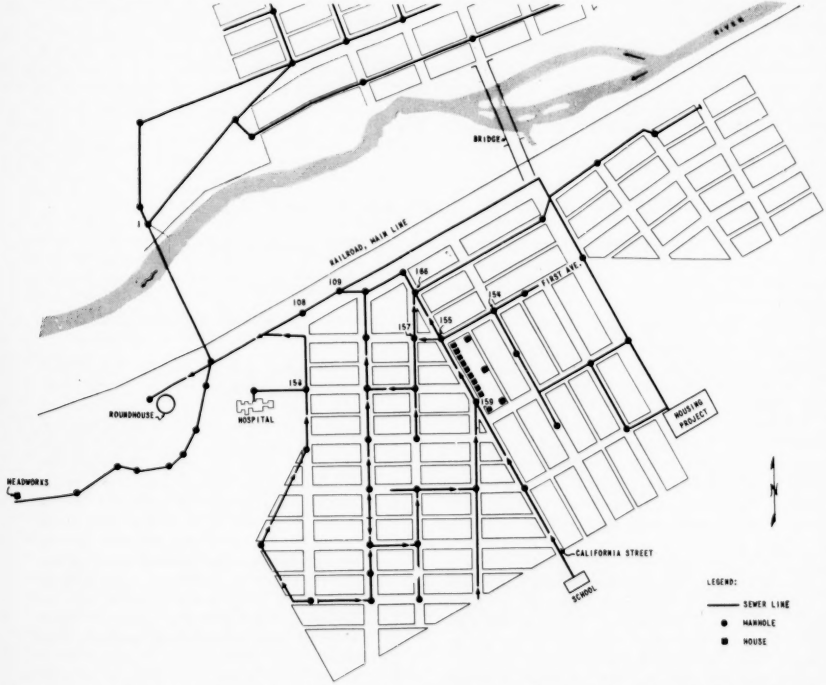
sewage sampling method was presented to the department in the summer of 1956. In and near a city of 2,200 population in the High Sierra country of California, a small but intermittent number of cases (four in five years) of typhoid had been reported over the preceding several years without discovery of the source of the infection. Because of the cooperation offered by the local governing and health officials and an engineering knowledge of the sewer system, it was felt that this community represented an excellent site for such a study. The major industries were railroading and lumbering. In addition, because of the plans to develop this community into a resort center, it was felt advisable to locate the possible carriers with as little contact as possible with the general public. A team consisting of physicians, nurses, microbiologists, and sanitary engineers was formed to make this study. The epidemiologic story is recounted here. Details of specific laboratory techniques will be reported elsewhere.[3] The sanitary engineering aspects have been reported by Greenberg, Wickenden, and Lee.[4]

Method of Study

Since there was no information available which would suggest the area in which the carrier (or carriers) resided, it was necessary to hold the entire town suspect. Even this assumption was somewhat dubious since the possibility could not be ruled out that the source of the cases was an itinerant, possibly a railroad worker. Preliminary work consisted of studying maps of the sewage system of the city and locating and opening certain manholes which appeared to be in key locations. Difficulties were encountered in finding some of the manholes which were covered with earth or asphalt. In these cases, a mine detector was used to locate the manhole. Other manholes were "dry," a result of obstructions in the lines, while others which were on the maps apparently did not exist at all.



Map of principal sewer lines and manholes in city where sewage sampling was done and discovery made of typhoid carrier.

When the preliminary work was completed, a mobile bacteriological laboratory was brought to the site of the investigation. Swabs consisting of pieces of fine mesh surgical gauze folded into eight

thicknesses, 6 in. long by 4 in. wide, were prepared. These were attached to strings and placed in the sewage stream at manholes which were selected to provide a survey of the Salmonella content of the entire sewage system. The figure shows the principal sewer lines and location of manhole 108. The swabs were removed after 48 hours and taken to the mobile laboratory where they were examined by the method of Moore and co-workers,[1c] as modified by the Division of Laboratories of the California Department of Public Health.

On July 9, only three days after the sampling began, a culture positive for Salmonella typhi was obtained from the head works (see figure) of the sewage system. While it had no value for localization, it was encouraging to know that there was probably a typhoid carrier in the community and that the method was capable of detecting his presence. There were no further findings of S. typhi until July 14, on which day the swab in manhole 157 yielded a positive culture. A day later, July 15, the swab in manhole 108 was found to be positive, and on July 16 positive cultures were obtained from manholes 109 and 166. During this period daily swab samples were collected from selected manholes in the northern portion of the city and from manhole 1, through which the entire sewage flow from that part of the city passed. These swabs were consistently negative and as a result further work was limited to the southern portion of the city, although surveillance was maintained at manhole 1.

When the presence of a typhoid carrier had been indicated, the field investigation was suspended temporarily, so that further plans could be developed for research purposes and additional characterization of the organism which had been found could be obtained.

Phage typing, which was considered essential, was attempted in our laboratory by multiple pickings from each culture, but the organisms were found to be "untypable" by phages at our disposal, although they all appeared to be identical and to belong to group D. Cultures were then submitted to Dr. Philip R. Edwards of the Communicable Disease Center of the United States Public Health Service in Atlanta, Ga., who reported all organisms to be members of phage group D. However, in addition to the lysis of phages which placed the cultures in group D, the cultures were lysed by a phage identified as Utrecht 9 described by Scholtens.[3] This phage type had been found by Scholtens in two epidemics and a few isolated cases in Holland and is not known to have been reported from any area in the United States. In view of this successful typing, a culture isolated from an acute case of typhoid in the area during the previous year and reported then as "untypable," was resubmitted to the Communicable Disease Center. Interestingly enough, it was also typed by Utrecht 9. After the clinical illness this patient had been released from surveillance with a negative stool culture. At the time of the study, control swabs were placed in the manhole outlet through which sewage flowed from the household of this known ex-case. All of these swabs were negative.

In August the field crew and mobile laboratory returned and active sampling was resumed. On the 5th, 6th, 16th, 17th, and 18th of August, the swab from 156 was positive for S. typhi. On the 16th, swabs from manholes 157 and 155 were also positive. As seen from the figure, the sewage from the hospital and part of the southwest section of the city passed through manhole 156. The flow from this manhole, as demonstrated by placing dye in the hospital sanitary system, is direct to the main line of the sewer system.

Swabs from manholes 159 and 154, both of which drained into 155, remained negative while under constant surveillance. This tended to place the carrier somewhere in the immediate drainage area of manhole 155, which is the most distant point in the system from which positive findings were obtained. Swabs were then placed in manhole 155 in such a manner as to get separate samples of the flow from the two feeding sewers. The swab from the California Street sewer was positive while the swab on First Avenue remained negative. This further located the carrier on California Street between manholes 155 and 159, which area involved only the small group of homes shown on the map.

Since the phage type identified had previously been reported only from Holland, we attempted to determine if anyone from this block had resided in Holland and/or had symptoms of typhoid. A roster was prepared of patients and staff present in the hospital during the period that positive findings were obtained in manhole 156. This was compared with the list of people living in the suspect block. One individual was found to have a common link and to fit this pattern. Inquiry then revealed a 77-year-old retired railroad worker who had been in the hospital for the treatment of hypertension and congestive heart failure during the period that typhoid had been isolated from the hospital manhole and who also lived in the suspected residential area. During his hospitalization he was treated for cardiac disease, but his role as a typhoid carrier was not suspected. He came to this country from Germany 50 years ago and both before and after had traveled extensively as a sailor. While in Germany he had lived in the same house with a person from Holland who was known to have typhoid. The patient stated, however, that he had never had any symptoms of the disease himself. Stool specimens were obtained from him and readily yielded S. typhi, of the same phage pattern as the cultures isolated from the sewers, thus confirming him as the carrier being sought. The carrier was hospitalized Aug. 3 to 18. In view of the evidence presented by Harvey and Phillips [2a] that S. paratyphi B may sur-

vive for periods of 10 weeks in sewers in the absence of contamination, a positive sample from 155 on the 16th was considered possible.

Comment

One of the principal advantages of the method presented herein is the localization of carriers of enteric disease without invasion of the household or of the privacy of individuals and without undue public alarm. Just how far it is possible to proceed in localizing individual carriers depends on such variables as the construction of sewer systems and access to manholes. In Sidmouth, England, where Moore [1a] made his studies, it was possible to place swabs in access holes of individual house drains, thereby localizing the source to individual houses. On the other hand, presence of houses with individual privies or cesspools would preclude such a method of mass surveying, unless, of course, there was seepage into a stream or other body of water which in turn could be tested by the swab technique.

In this study it was felt that the practical limit of usefulness of the sewer system survey had been reached when the carrier was localized to one block. However, at this point, several methods for the further pinpointing of the source without any intrusion upon the population were apparent. The first and most attractive of these alternatives was previously described; the utilization of the limited geographical distribution of the phage type of the isolated organism. Although phage typing is an essential part of an epidemiologic study of a typhoid outbreak, this to our knowledge is the first time that the phage type presented the clue that led to the presumptive description of the carrier.

Another procedure was considered but not found necessary to use in this particular situation. This would have been to pass a line to which was attached a number of swabs through the sewer in the direction of sewage flow so that one swab rested in front of each house. By withdrawing the line at the insertion point it should have been possible to detect the house which presumably was the source of the Salmonella, since it should be at the point of the first positive swab on the line. Should all indirect methods have failed it would, of course, have been possible to interview and collect stool specimens from the individuals in the limited number of suspected houses. Similarly, swabs could have been placed in individual toilets, then collected and cultured, as was done by Kwantes and Speedy.[6] This was actually performed in the town after the conclusion of the major portion of the project, and positive findings showed that this too would have been epidemiologically feasible.

Since this project was initiated as a study in methodology, other problems were investigated. One was to determine if grease which commonly accumulates on the insides of the sewers could act as a trap for the typhoid organisms, as has been suggested by Harvey and Phillips [2a] and by Browne and Greenberg.[7] The latter found that an appreciable number of sewer grease samples which had been washed up on beaches near sewer outfalls were contaminated with Salmonella. Accordingly, samples of floating grease, as well as "wipes" of the walls of accessible pipes, were obtained. A significant number of positive findings were made by this method, especially by the wipes. Further studies are under way on the value of direct grease sampling. If this proves successful it would eliminate the time and labor necessary for placing and removing swabs. It would also serve as an index of the Salmonella present in the sewer prior to the start of the studies.

Another question which was studied was the possibility of sending the samples directly to the State Central Health Department Laboratory, in this case 200 miles from the site. Duplicate swab samples were taken and one was analyzed in the mobile laboratory while the second was shipped by express to Berkeley in a portable icebox. On only one of the 275 duplicate samples submitted did the two laboratories differ in their findings.

Summary

A study was made of the feasibility of searching for typhoid carriers by culturing samples of sewage taken at different points within a city. In this instance, it was possible to localize the residence of a carrier to a single block. Further localization was rendered unnecessary when positive specimens were found in the sewage outflow from the community hospital and the name of a resident of the suspected block was found in the hospital roster. Direct stool cultures from this man showed him to be a typhoid carrier, and phage typing of the organisms indicated that he probably had acquired his infection many years previously in Europe. Localization was also accomplished by household toilet swabs. The method has proved feasible as a practical field study technique.

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FAILURE OF PENICILLIN IN TREATMENT OF ACUTE GONORRHEA IN AMERICAN TROOPS IN KOREA

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The results of treating patients with acute gonorrhea by five daily intramuscular injections of 600,000 units of procaine penicillin G were followed up in 148 men. The treatment failed in 30. In 13 of these a second course was given. It was successful in nine, and in the four cases of failure cure was obtained with oxytetracycline. In 17 men the initial course of penicillin which failed was followed by treatment with oxytetracycline; this was successful in 15 cases, and in the 2 men who were not cured by it treatment with chloramphenicol was successful. Two cases of failure of penicillin are cited to illustrate the course of the infection. The present high rate of failure with repeated doses is in marked contrast to the much lower rate of failure with single smaller doses reported elsewhere two years ago. This evidence that a penicillin-resistant strain of Neisseria gonorrhoeae has emerged is of grave significance.

The remarkable response of gonorrhea to penicillin has long been emphasized, and it is usually held that penicillin-resistant Neisseria gonorrhoeae do not appear. However, in Korea failure of gonorrhea to respond to an adequate course of penicillin treatment is not uncommon. Not infrequently, military physicians in Korea encounter in soldiers cases of acute gonorrhea which persist in spite of 5 or even 10 daily injections of 600,000 units of an aqueous solution of procaine penicillin G.

Materials and Methods

This paper is a report of failures of penicillin therapy in cases of acute gonorrhea among United States troops in Inchon, Korea. Inchon is a major Korean port with about 2,000 military personnel, nearly all Army, receiving medical care from the Army dispensary. The study covers a three-month period, from Jan. 1 to April 1, 1958, during which 165 cases of acute gonorrhea in these troops were treated. An adequate follow-up study was possible in 154 cases, and this is the number of cases analyzed. Since the only reason for inadequate follow-up study was the movement of patients to another area, discounting these cases should not bias the results.

All cases represented acute gonorrhea with sudden onset of a purulent urethral discharge. In every case a history of recent sexual intercourse was obtained. Eight patients in this series had two cases of gonorrhea during the three-month period; therefore, a total of 146 persons were involved. These eight cases were felt to be reinfections and not treatment failures, since all of the patients had been asymptomatic for a period of at least two weeks after completing treatment and in seven of the eight a history of sexual intercourse after treatment was elicited.

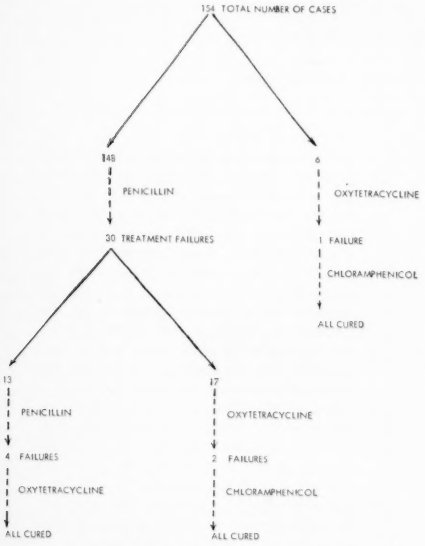
Diagnosis.—The diagnosis of gonorrhea was made by the demonstration of characteristic biscuit-shaped, gram-negative, intracellular diplococci in Gram-stained urethral smears. All smears were examined by the same experienced technician. Smear findings in all cases of failure of treatment were confirmed by myself.

Treatment.—All patients with gonorrhea were given a printed sheet of directions and also instructed verbally to (1) be sure to take all five injections of penicillin, (2) return for reexamination three days after the last injection, and (3) abstain from alcohol and intercourse for two weeks. They

were also given two weeks of medical restriction to their compound. No restrictions of other physical activities or exercise were imposed.

Except for those with a history of penicillin allergy, all patients received five daily intramuscular injections of 600,000 units of an aqueous suspension of crystalline procaine penicillin G. Only penicillin well within the expiration date was used.

Patients allergic to penicillin received a course of oxytetracycline therapy, 500 mg. four times a day for four days and then 250 mg. four times a day for three days. Patients treated with chloramphenicol were given 500 mg. four times a day for four days.



Type of treatment and results in 154 acute cases of gonorrhea.

Follow-up Study.—In order for the results of therapy to be evaluated, patients were entered on an injection record and this was checked daily for missed injections. Patients who failed to take the injections were called in and scheduled for additional injections to give a total of five treatments.

Any patient who was asymptomatic and free of discharge on examination three or more days after his last injection was considered cured. If a slight discharge persisted, at least two and usually three smears on different days had to give negative findings for N. gonorrhoeae before the patient was considered cured.

Results

The type of treatment and the clinical results are illustrated in the figure. In one of the six patients receiving oxytetracycline a relapse occurred and a course of chloramphenicol therapy was required for cure. Of 148 persons who received penicillin, 30 were not cured.

These 30 patients in whom penicillin treatment failed were divided into two groups, with 17 receiving oxytetracycline and 13 given a second course of penicillin therapy. Of these 13, 4 were not cured by this second course. They subsequently responded to a course of oxytetracycline therapy. In the group of 17 treated with oxytetracycline, 2 were not cured. Both were successfully treated with chloramphenicol.

In none of the 30 patients in whom penicillin treatment failed could a history of further sexual contact be obtained, even with careful inquiry. In two cases some doubt remained as to whether reinfections rather than treatment failures had occurred, since the interval between the last injection and the finding of a smear positive for N. gonorrhoeae was 11 and 13 days, respectively—considerably longer than in the other instances.

In the other 28 patients the time between the last injection and demonstration of positive smear results varied from zero to eight days, with an average of four days. In 14, N. gonorrhoeae was demonstrated in the smear zero to three days after the last penicillin injection. This interval could probably have been reduced somewhat with closer follow-up examinations of patients, since not infrequently a discharge had been present for a few days before the patient reported it.

Failure to receive all penicillin injections cannot account for the 30 instances of relapse, since only two patients missed one injection while two others missed two injections. These injections were made up, but a lapse of one or two days in the course of treatment in these four patients did result.

One interesting observation in the patients in whom penicillin treatment failed was that the character of the discharge often changed from thick and purulent to relatively thin and mucoid. The clinical picture changed from that of acute gonorrhea to one resembling nongonorrheal urethritis or chronic gonorrhea. Also, not infrequently a smear done early in the stage of treatment failure would be negative, while on repeat smear a day or two later myriads of typical intracellular diplococci would be apparent.

In 140 of the cases it was possible to examine the charts one month later for complications. There were eight penicillin reactions, an approximate incidence of 5%. All of them were mild, the chief manifestation being urticaria. Nongonorrheal urethritis occurred in 16 or about 10% of the cases. Ad-

ditionally, there were two cases of epididymitis, one of prostatitis, and one of sterile injection site abscess.

Report of Cases

In most of the patients with treatment failure the discharge disappeared after one or two injections, only to return after treatment had been completed. The following case is typical.

CASE 1.—An 18-year-old boy was seen on Jan. 29, 1958, with a purulent urethral discharge which had begun the day before. He had had frequent sexual contacts, the most recent being four days previously. A smear proved positive for N. gonorrhoeae, and he was given a course of penicillin therapy. Three days after his last injection he reported with a small amount of moderately thick discharge. He denied further intercourse. Check of injection records revealed he had received all five injections. He stated that the discharge stopped on the second or third day of treatment but returned two days after his last injection. The smear was positive for N. gonorrhoeae. He was given a second course of penicillin treatment, and a final examination two weeks later revealed him to be asymptomatic and free of discharge.

In some of the failures the discharge diminished but did not disappear under treatment. In a few of these cases it was possible to demonstrate N. gonorrhoeae in the discharge while the patient was undergoing treatment. Details in one of these cases are given below.

CASE 2.—A 23-year-old man reported with a purulent urethral discharge on Feb. 10, 1958. He had been stationed in Korea since May, 1957, but had had no previous venereal disease. The discharge began the evening before, sexual intercourse having occurred six days previously. A smear was positive for N. gonorrhoeae. A course of penicillin therapy was prescribed. He returned on the fifth day of treatment with a persisting discharge which was positive for N. gonorrhoeae. He had received all five injections. He was given an additional five days of penicillin therapy. On the 10th day of penicillin treatment (Feb. 19), he reported that his urethral discharge had not disappeared. Smear revealed numerous pus cells and extracellular gram-negative diplococci but no intracellular forms. A repeat smear the next day was positive for N. gonorrhoeae. A course of oxytetracycline therapy promptly cleared his discharge. A final examination 18 days later (March 10) revealed him to be asymptomatic and free of discharge.

Comment

A 20% treatment failure rate is both unusual and unsatisfactory. Gjessing [1] reported a relapse rate of only 2.9% in 1,115 male patients with acute gonorrhea treated by the venereal department of the Bureau of Public Health, Oslo, Norway. A single injection of 300,000 units of procaine penicillin G was employed. In a series of 424 men treated similarly by the venereologic outpatient department of Marselisborg Hospital, Aarhus, Denmark, Nørgaard [2] reported 5% as having recurrences. Lodin [3] noted one recurrence among 78 Swedish male military recruits treated in the same way.

In the studies cited above the treatment failure rate varied from 1 to 5%; yet, although we used 10 times as much penicillin, 20% of our patients were not cured. That individual variation in penicillin metabolism, exercise, and alcohol consumption cannot account for this discrepancy is clear, since all these series involve mainly young males treated as outpatients.

The question that arises is whether these cases represent gonorrhea or some other disease. That is, how accurate is our diagnosis? The fact that bacterial culture studies were not done will no doubt be held, by some, as contributing to failure to establish the diagnosis. In males the finding of typical gram-negative intracellular diplococci is a practically absolute diagnostic criterion.[4] As Pelouze [4] and others have pointed out, all these criteria must be rigidly adhered to, since urethral exudates are frequently filled with extracellular, and even occasionally intracellular, cocci other than N. gonorrhoeae. To insure a correct diagnosis, I insisted that only a smear showing intracellular, gram-negative diplococci, of typical morphology, could be labeled as positive for N. gonorrhoeae.

Without a doubt, cultures would have been helpful. But the value of cultures for N. gonorrhoeae in a male is not to confirm a positive smear but to detect those cases of gonorrhea which yield a negative smear. Therefore, any error introduced by relying only on smears would give a falsely low value for the number of treatment failures. In an attempt to overcome this handicap, repeated smears were done on post-treatment discharges which were negative for N. gonorrhoeae at the first follow-up smear. However, no doubt an occasional case of post-treatment discharge labeled as nongonorrheal urethritis may have been an undetected treatment failure.

If, indeed, the treatment failures represent persistent gonorrhea, what evidence is there that these are not reinfections? It is, of course, impossible to prove that reinfection could not have occurred in each and every treatment failure. In order to rule out reinfection as far as possible, all patients were restricted to army compounds for two weeks and carefully questioned regarding further sexual contacts. Patients with gonorrhea are quite anxious while undergoing treatment, and, for a short while at least, follow instructions. These considerations do not rule out the possibility that an occasional treatment failure was the result of reinfection. However, they do eliminate reinfection as an explanation for the 20% failure rate.

It should be pointed out that reinfection cannot possibly explain treatment failures in patients in whom N. gonorrhoeae was demonstrated in the discharge while the patient was on penicillin treatment. The daily dose of penicillin used is several times as great as the amount needed for effective prophylaxis of gonorrhea.

Failure of penicillin in the treatment of gonorrhea is a common experience in the Far East. The chief of the urology service at the U. S. Army's

121 Evacuation Hospital in Korea has frequently encountered penicillin treatment failures.[5] Kern [6] reported nine failures in 59 consecutive cases of gonorrhea treated in the port city of Pusan, Korea. Treatment was identical with that used in this study. Sabath [7] had a failure rate of over 30% among troops in the First Cavalry Division area in Korea treated with three daily injections of 600,000 units of procaine penicillin G in oil with 2% aluminum monostearate.

It seems to me that these cases of penicillin treatment failures can only be explained on the basis of penicillin-resistant strains of N. gonorrhoeae. When referring to penicillin resistance, increased relative resistance is meant. That is, a significantly higher concentration of penicillin is required for an antibacterial effect than is the case with usual strains of N. gonorrhoeae. Surprisingly, until recently there were practically no reports on penicillin-resistant N. gonorrhoeae in the literature.

From Great Britain, King [8] reported in March, 1958, "There is evidence that penicillin-resistant strains of gonococci are now emerging. Some cases of acute gonorrhœa fail to make any response to doses of penicillin which in the past were nearly always highly efficacious. Repeated doses of penicillin and doubling the doses may have no effect. In other cases, response seems satisfactory but relapse follows within a day or two. Quantitative in-vitro tests for sensitivity to penicillin suggest that in these cases organisms from the secretions are considerably less sensitive to penicillin than the Oxford staphylococcus or other strains of gonococci."

Cradock-Watson and co-workers [9] noted an apparent increase in penicillin treatment failures in England in a recent report of 200 cases. In vitro sensitivity studies, when compared to the clinical results, showed most of the failures to be in the relatively small group of patients who were infected with the more penicillin-resistant strains.

Bernstein [10] recently completed a thorough study of the bacteriology of penicillin treatment failures among United States military personnel in Japan. He demonstrated in vitro resistance of certain strains of N. gonorrhoeae to penicillin. Furthermore, the results of these in vitro sensitivity studies, when combined with blood penicillin level determinations, correlate well with the clinical course of the patients with penicillin treatment failures. He has shown that those in whom penicillin treatment has failed can be cured with penicillin providing it is administered in doses which raise the blood penicillin level sufficiently to overcome the penicillin resistance of N. gonorrhoeae. Bernstein also considers the repository form of penicillin to be of little value, since it does not raise the blood penicillin level sufficiently.

Although many authorities recommend treatment of acute gonorrhea in the male with a single injection of 600,000 units of repository penicillin, this has been abandoned by most military physicians in Korea. I have found procaine penicillin G in oil with 2% aluminum monostearate disappointing. Not only are treatment failures more common, but the clinical picture is obscured by the more prolonged suppressing action of the repository form of penicillin.

In this study, oxytetracycline was used a total of 23 times, with three failures. I believe that these failures are due to resistance of N. gonorrhoeae rather than to the patient's failure to take the medicament. When used in amounts of 2 Gm. daily, in divided doses, broad-spectrum antibiotics not infrequently fail to cure when penicillin treatment has failed. Others have had the same experience, even though this treatment was continued for seven days.[11] Although, in my experience, chloramphenicol had cured about 10 times when penicillin had failed, Romsey,[5] as well as Bernstein,[10] have reported occasional failures with chloramphenicol.

From the clinical standpoint, the emergence of penicillin-resistant strains of N. gonorrhoeae has grave significance. No longer can acute gonorrhea be considered lightheartedly as a disease with a certain cure and less disability than a common cold. The twin problems of chronic gonorrhea in the male and the asymptomatic male carrier, which had been largely banished by penicillin, have returned. It is probably only a matter of time until penicillin resistance will be met on an increasing scale all over the world. Furthermore, careful and prolonged follow-up studies will be necessary. In all likelihood various types of "provocative" tests will again have to be performed to ascertain a cure.

Summary

Among a series of 146 male military personnel treated for acute gonorrhea in Inchon, Korea, 30 (20%) failed to be cured by a course of five daily injections of 600,000 units of crystalline, aqueous, procaine penicillin G. It is felt that increased penicillin resistance on the part of Neisseria gonorrhoeae is the probable cause of these failures. Since penicillin may produce a suppressing, but not curative, action on gonorrhea, careful follow-up studies are important.

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Joseph Dressler supplied technical assistance in this study.

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CLINICAL NOTES

SCREENING FOR DIABETES BY THE GLUCOSE OXIDASE METHOD

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Recently there has been increasing interest in screening programs for diabetes, and several different screening methods have been advocated.[1] The results of screening programs differ considerably, depending on the age, weight, and family history of the group screened; on the type, technique, and standards of screening; on the extent of diagnostic evaluation; and on the diagnostic criteria for diabetes mellitus used in the program.[1a]

Although there is disagreement as to the choice of a screening procedure, certain general principles are acceptable to most authorities.[1e] It is generally recognized that, while the glucose tolerance test would be the ideal procedure, it is too expensive and too complicated for most large-scale programs. The combination of a urine sugar test and a postprandial blood sugar test is considered to be one of the most effective methods, but this has a limited application because of the necessity of obtaining a blood specimen. It is obvious that the urine sugar test is simpler and less expensive than the above procedures. However, heretofore only the copper reduction method has been available. This test is not specific for glucose, giving positive results with fructose, lactose, and other reducing substances.[1e] In addition, this technique tends to detect frank diabetes but to overlook mild or latent cases in which early treatment may be indicated.

Recently, specific enzymatic tests for glucose have become available.[2] These enzymes are flavoproteins which catalyze the aerobic oxidation of glucose to gluconic acid with the production of hydrogen peroxide. The presence of glucose in urine is detected by color changes of reagent-treated paper. The enzyme tests are specific for glucose in amounts as small as from 0.01 to 0.1%. Negative results have been obtained in the presence of lactose, fructose, xylose, mannitol, acetylsalicylic acid, amphetamine, barbiturates, sulfonamides, quaternary ammonium compounds, and hexylresorcinol. In view of the specificity of these tests for glucose, it was considered worthwhile to conduct a detection survey utilizing them in comparison with a copper reduction method.

Attending Physician, Grant Hospital and Clinical Assistant Professor, Department of Medicine, University of Illinois College of Medicine (Dr. Chertack), and Pathologist, Grant Hospital of Chicago, and Clinical Assistant Professor of Pathology, University of Illinois College of Medicine (Dr. Sherrick).

Materials and Methods

The survey was held during Diabetes Detection Week. A booth was set up in the lobby of the University of Illinois Research and Educational Hospitals, and personnel associated with the professional schools were urged to bring a urine specimen to the booth one hour after a full meal. The specimens were tested for reducing substances by a commercial copper sulfate tablet test (Clinitest) and for glucose by two glucose oxidase tests (Clinistix and Tes-Tape). If the result of any one of the three tests was positive, a glucose tolerance test was done. The "true glucose" method of Somogyi-Nelson[3] was used for determination of the blood glucose level, and the glucose tolerance test was done as follows: a fasting venous blood specimen was obtained, a calculated dose (1 Gm. per kilogram of body weight) of glucose was given orally, and venous blood samples were obtained at intervals

of one-half, one, and two hours. The criteria used for the diagnosis of diabetes were those of Mosenthal,[4] i. e., a fasting blood glucose level of more than 100 mg. per 100 ml., a one-hour level of more than 150 mg. per 100 ml., and a two-hour level of more than 100 mg. per 100 ml.

Results

In all, 742 urine specimens from as many individuals were examined. In 30 cases, positive results with one or more techniques were obtained. These 30 persons were recalled, and evaluation was done for diabetes mellitus. The data obtained are summarized in table 1. The first 11 patients are diabetics, with the disease previously unknown in 8. Five patients had borderline glucose tolerance findings and are classified as "doubtful normal." This group has been called prediabetic, latent diabetic, hidden diabetic, or possible diabetic, and such patients should be watched for possible future development of diabetes.[5] Six patients had non-glucose-reducing substances in their urine specimens. Two had renal glycosuria. There were six normal persons.

A comparison of the results of the tests is shown in table 2. Here it can be seen that diabetes in 2 of the 11 subjects was detected by the glucose oxidase methods but not by the copper sulfate method. Two of the five doubtful normal persons had positive findings in the glucose oxidase tests only. Of the six urine specimens containing non-glucose-reducing substances, positive results were obtained only by the copper sulfate method; none were positive by either of the enzyme methods. One case of renal glycosuria was detected only by the glucose oxidase method. Of the six normal subjects, five showed positive findings in the glucose oxidase method and one in the copper sulfate method.

Thus, of 18 subjects including 11 diabetic persons, 5 doubtful normal persons, and 2 persons with renal glycosuria, negative results were obtained in 5 by the copper sulfate method. Positive results were obtained in all by the glucose oxidase method. Of 12 subjects without diabetes, positive results were obtained by the copper sulfate method in 7 (6 with non-glucose-reducing substances and 1 doubtful normal person). Positive results in the glucose oxidase tests were obtained in five subjects who had normal glucose tolerance findings.

TABLE 1.—*Clinical and Laboratory Data in Evaluation of Positive Findings in Screening Test for Diabetes*

Case	Age, Yr.	Family History of Diabetes	Previous Glycosuria	Weight, Lb.	Clinitest* 2 Drops	Clinitest* 5 Drops	Tes-Tape†	Clinistix†	Glucose Tolerance Fasting	30-Min.	60-Min.	90-Min.	120-Min.	Comment
1	43	+	+	165	2+	2+	1/2	+	...	...	...	...	...	Known diabetes
2	30	+	+	135	2+	2+	1/2	+	...	...	...	...	...	Known diabetes
3	53	—	+	190	—	1/4	1/10	+	141	...	...	...	...	Known diabetes
4	57	+	—	188	±	1/4	1/10	+	97	160	208	151	85	Diabetes
5	18	+	—	153	—	1/4	1/10	+	96	162	148	88	73	Diabetes
6	24	—	+	160	—	1/4	1/4	+	102	168	180	121	59	Diabetes
7	49	—	—	167	—	—	1/10	+	106	174	238	84	60	Diabetes
8	55	—	+	200	2+	2+	1/2	+	188	...	...	...	...	Diabetes
									101	141	179	123	99	
9	37	+	—	153	—	1/4	1/10	+	82	123	180	159	93	Diabetes
10	50	—	—	133	—	—	1/10	±	85	213	200	138	68	Diabetes
11	45	—	—	145	1/4	+	1/10	±	100	165	190	144	78	Diabetes
12	23	—	—	145	1 1/2	+	1/2	+	94	142	158	96	80	Doubtful normal
13	45	—	—	179	—	—	1/10	±	91	152	107	68	79	Doubtful normal
14	19	—	—	175	—	—	1/10	+	89	143	157	131	76	Doubtful normal
15	29	—	+	134	—	1/4	1/10	+	90	150	123	64	84	Doubtful normal
16‡	57	—	+	170	3/4	1/2	1/2	+	...	...	...	...	...	Doubtful normal
17	64	—	—	...	—	1/4	—	—	...	...	...	...	...	Non-glucose-reducing substance
18	34	—	—	140	—	1/4	—	—	...	...	...	...	...	Lactose
19	54	—	—	122	1/2	1/2	—	—	...	...	...	...	...	Non-glucose-reducing substance
20	32	—	—	118	—	1/4	—	—	...	...	...	...	...	Non-glucose-reducing substance
21	30	—	—	135	—	1/4	—	—	...	...	...	...	...	Lactose
22	20	—	—	112	—	1/4	—	—	...	...	...	...	...	Non-glucose-reducing substance
									59	71	75	73	79	
23	26	—	—	120	3/4	1	1/2	+	78	106 Urine+	101	83	75	Renal glycosuria
24	40	—	—	200	—	—	1/10	±	91	128 Urine+	97 Urine+	56	90	Renal glycosuria
25	28	—	—	150	—	—	1/10	—	92	149	84	81	78	Normal
26	24	—	—	170	—	—	1/10	±	81	139	104	73	82	Normal
27	68	+	—	180	—	1/4	1/10	—	...	...	...	...	...	Normal
28	22	+	—	162	—	—	1/10	±	91	122	106	102	111	
									90	116	108	100	90	Normal
29	19	—	—	155	—	—	1/10	±	95	135	90	105	97	Normal
30	46	—	—	160	—	—	1/10	±	91	130	114	65	62	
									92	136	153	90	50	Normal

* Copper sulfate tablet test.
† Glucose oxidase test.
‡ Abnormal glucose tolerance test; details not available (family physician).

Comment

Screening procedures for diabetes are judged on specificity and sensitivity.[1e] Sensitivity, meaning that a high percentage of persons with the condition should show positive results, was high with the glucose oxidase tests in this survey. In any screening program, it is not possible to know how many subjects actually have diabetes mellitus. Therefore, sensitivity must be estimated by comparing percentage screened who have positive findings in this study with that in other studies. The result of 4% compares favorably with the 86,865 individual examinations collected from several surveys by Wilkerson and co-workers,[1e] in which the average was 2.1%, with a range of 1.3 to 9.0%. In all of these studies a test of blood sugar level was utilized as the screening procedure.

TABLE 2.—*Comparison of Tests with Positive Results in Detection of Diabetes*

Test	Subjects, No.					
	Total	Diabetic	Doubtful	Non-glucose-Reducing Substance	Renal Glycosuria	Normal
Total	30	11	5	6	2	6
All 3 methods	13	9	3	...	1	...
Clinistix* and Tes-Tape*	9	2	2	...	1	4
Clinitest† and Tes-Tape	1	...	...	...	...	1
Clinitest alone	6	...	...	6	...	...
Tes-Tape alone	1	...	...	...	...	1
Clinistix alone	0	...	...	...	...	...

* Glucose oxidase test.
† Copper sulfate tablet test.

Of the total group screened, 1.5% had diabetes. This also compares favorably with respect to sensitivity with the collected average percentage of Wilkerson and associates of 0.5% (range, 0.2-2.0%). Another indication of the relatively high sensitivity of the study is shown by the fact that 36% of those screened with positive results had diabetes, which compares favorably with the average of Wilkerson and associates of 24%, with a range of 22 to 64%.

The criterion of specificity, i. e., that a high proportion of persons not having the condition should show negative findings, is fulfilled at least as well by the enzyme tests as by the copper reduction method. According to the diagnostic evaluation, 12 of the 30 subjects with positive results on screening were probably entirely normal. In this group, seven positive results were obtained only with the conventional copper sulfate method and five only with the glucose oxidase tests.

Thus, the glucose oxidase tests were demonstrated to be satisfactory screening methods for diabetes mellitus. Although sensitivity is higher than with the copper sulfate method, the number of false-positive results is no greater; it is considered that the early detection of diabetes mellitus is enhanced by the use of glucose oxidase tests. Since it has been established that transient glycosuria frequently precedes diabetes,[5b] the high sensitivity of the new methods may be of value in detecting persons with doubtful cases of diabetes who should have periodic evaluation.

Summary

Two glucose oxidase tests for glycosuria were compared with a copper reduction method in screening 742 subjects for diabetes mellitus. Of 30 persons with positive findings on the screening tests, 11 had diabetes. The glucose oxidase tests were more sensitive and more specific for glycosuria than the copper sulfate method. The results are comparable to those obtained in surveys where a test of blood sugar level is utilized as the screening procedure.

840 S. Wood (12) (Dr. Chertack).

The copper sulfate tablet test (Clinitest) and one of the glucose oxidase tests (Clinistix) used in this study were supplied by Ames Co., Inc., Elkhart, Ind. The other glucose oxidase test (Tes-Tape) was supplied by Eli Lilly and Company, Indianapolis.

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NEW INSTRUMENT FOR BIOPSY OF THE CERVIX AND ENDOCERVIX

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and
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The perfection of cytological techniques in the detection of early carcinoma of the cervix has necessarily required the widespread use of cervical biopsy for confirmation. The frequent small size of the lesions, their clinically inconspicuous appearance, involvement of the endocervix, and the ease with which they may be destroyed, lost, or rendered undiagnosable by the usual techniques of biopsy have indicated the development of new instruments and methods.

When carcinoma is strongly suggested by cytology but the cervix is clinically free of an obvious lesion, the cold cone is recommended to confirm the diagnosis and define its extent and aggressiveness. However, especially in pregnancy, often reports are given of "cells suspicious of malignancy" or "inconclusive findings," their frequency depending on the competence, self discipline, and philosophy of the cytologist. Here, a less rigorous procedure is permitted, avoiding the disadvantages of hospitalization and the risks of hemorrhage and stenosis. Toward this purpose, a new cervical biopsy instrument termed the Cervicotome is presented. It is designed to obtain tissue specimens from the portio vaginalis, the squamocolumnar junction, and the cervical canal (a "pancervical" biopsy).

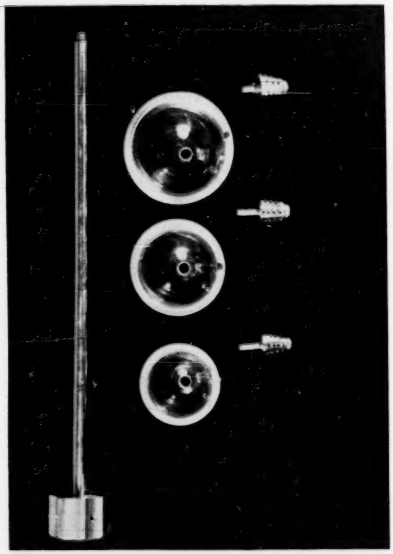

Fig. 1.—Cups, matched blades, and coaxial cutting plug attachments, of several sizes, of biopsy instrument. These are designed to accomodate variations in size of cervix, cervical os, and cervical canal.

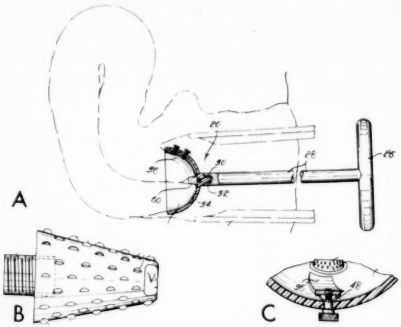

Fig. 2.—*A*, operating position of biopsy instrument, with coaxial cutting plug in cervical canal (60) and cutting blade (36) in contact with cervix. *B*, enlarged drawing of coaxial cutting plug, showing multiple cutting teeth. *C*, detailed drawing of Lucite cup, razor-edged cutting blade (36), and micrometer adjusting screw (48) which determines depth of cut.

This instrument is basically a hemispherical cup attached to an elongate handle. The cup includes an internal curved knife and a coaxial attachment, with multiple serrated cutting edges (fig. 1). The cup and knife are applied over the cervix to remove tissue from part or the entire surface of the cervix, from the external os to a major portion of the portio vaginalis. The concentric cutter will simultaneously obtain small specimens of epithelial and subepithelial tissue from the canal. The cup is made of Lucite to permit the operator to monitor the cutting action.

Operation and Results

With the cervix exposed with a vaginal speculum in place, the Lucite cup is applied to the cervix, with the concentric cutter attachment in the cervical canal (fig. 2). Appropriate pressure is applied to the handle of the instrument as it is rotated in a clockwise direction. Counterpressure may be applied to the fundus with the operator's left hand

on the abdomen, at the discretion of the operator. The instrument may be rotated a full 360 degrees where no gross lesions or ulcerations are present on the portio vaginalis.

The instrument may be used in conjunction with Schiller's test and in areas of exophytic growth or gross ulceration. It should be emphasized that the instrument is designed to perform a cutting, rather than a scraping, function. Thus, the physician obtains specimens for definitive histological diagnosis. The specimens obtained from the portio vaginalis and the cervical canal may be examined separately, so that the general location of the lesion will be indicated.

The material obtained is adequate for study, consisting of both squamous epithelial and endocervical tissue and including the junctional zone. The tissue is well preserved, showing less artifact than that obtained by other methods. Necessarily, it is representative of the entire circumference of the cervix, and sufficient lamina propria is obtained to judge infiltration of the stroma.

Summary

A new cervical biopsy instrument, the Cervicotome, is designed to obtain tissue from the portio vaginalis, the squamocolumnar junction, and the cervical canal in one rapid operation. Its use is intended for office practice on ambulant patients, where the cytological diagnosis has been reported doubtful or suspicious, where an infiltrative lesion is probable, or where the patient has refused hospitalization.

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COUNCIL ON DRUGS

Report to the Council

The Council has authorized publication of the following report. Nonproprietary terminology is used for all drugs that are mentioned; when such terminology is not considered to be generally well known, its initial appearance is supplemented by parenthetic insertion of names known to be applied to commercial preparations.

H. D. KAUTZ, M.D., *Secretary.*

CURRENT STATUS OF THERAPY IN BRONCHIAL ASTHMA

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Bronchial asthma is a distressing and common form of acute, recurrent, or chronic bronchial inflammation and obstructive emphysema, usually of allergic origin. The acute paroxysm of bronchial asthma may last for hours or recur in varying degrees of severity for days. Finally, a state of intractable asthma, during which the episode is continuous and refractory to treatment, may result. In this state the patient presents a picture of marked physiological imbalance. Evidence of hypoxia, cyanosis, dehydration, disturbed psyche, peripheral vascular collapse, and further disturbances may be noted because of changes induced by the widespread use of drug therapy. Death is more commonly due to asphyxia resulting from the plugged and obliterated bronchi and bronchioles and from oversedation; it is also due to the failure of endogenous discharge of adrenal hormones necessary in the defense mechanism against stress, and, in more recent years, particularly to steroid sequelae.

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Medical Management

The successful management of the patient with chronic bronchial asthma requires a very careful consideration of the responsible factors in bronchial asthma. Such factors include allergic factors (inhalants, ingestants, contactants, injectants), common colds, paranasal sinus disease, bronchitis (allergic, asthmatic), physical factors (seasonal and climatic influences), psychosomatic factors, and miscellaneous factors (exertion, fatigue, endocrine influence, nonspecific pulmonary irritants, infections).

Every attempt should be made to determine the responsible antigens. If a detailed history is inconclusive as to the cause of a patient's bronchial asthma, then scratch testing and intradermal testing may be resorted to. Removal of the offending allergen (allergic cleanliness) and a trial with specific hyposensitization should be promptly instituted in all cases whenever possible. Further therapy should be directed toward removing the contributory factors. Because search for the responsible agents is

difficult and often completely unsuccessful, emphasis on the allergic approach to management should not exclude physiological therapy.

Epinephrine.—Epinephrine has been employed in various modifications, concentrations, and routes. Toxic reactions, intolerance, and fastness are more commonly observed with overdosage and repeated parenteral use. Deaths have been reported after intravenous administration. In general, epinephrine given parenterally is limited in its value for the relief of the acute attack. Unfortunately, few physicians or patients limit the dosage to the proper and effective subcutaneous injection of 0.2 to 0.3 cc. of a 1:1,000 dilution of epinephrine hydrochloride. Generally, larger doses at frequent intervals are resorted to, especially when self-administered. The use of the hypodermic needle for self-medication is encouraged too often; the epinephrine-fast state is encountered most commonly in these patients. We have not observed any value from preparations of epinephrine 1:500 in oil.

Most patients in status asthmaticus are epinephrine-fast, and the repeated use of all epinephrine preparations should be avoided until epinephrine sensitivity is restored. We have made a rule of never adding epinephrine to the so-called intravenous cocktail (i. e., intravenous infusion of aminophylline, iodides, dextrose, etc.).

Bronchodilator Aerosols.—Aerosols of sympathomimetic drugs, such as 2.25% racemic epinephrine (Vaponefrin) hydrochloride, isoproterenol (Aludrine, Isuprel) hydrochloride 1:200, a combination of 2.5% racemic epinephrine hydrochloride with 0.5% atropine sulfate (Dylephrin), or a combination of 0.4% isoproterenol sulfate with 2% phenylephrine hydrochloride (Nebu-Prel) have proved to be of great value for the relaxation of bronchospasm. As little as approximately 0.05 to 0.10 cc., nebulized by three to six compressions of a hand bulb, may abort or relieve a mild bronchospastic episode. We have observed clinical and laboratory improvement with administration of these agents.

Recently, epinephrine and isoproterenol have been added to Freons in the form of simple pocket units (Medihaler-Epi and Medihaler-Iso) designed to deliver measured aerosol dosages. The Medihaler-Iso unit is popular with patients and produces improvement in timed vital capacity relationships as tested in those with mild or moderate attacks of bronchial asthma. The class of Freons used to power this has been described as free of toxicity. More recently, a Freon-powered pocket unit has become available with an ingenious reservoir chamber with a self-cleaning, baffling device (Nebu-Halent). This device makes it possible to deliver finer, smaller particle-sized aerosols of bronchodilator agents or other therapeutic aerosols as prescribed by the physician. We were able to determine that in mild paroxysms of bronchial asthma three inhalations with this device, and in moderately severe paroxysms six inhalations, brought effective clinical relief and improvement in timed vital capacity relationships.

More severe bronchospasm may require 0.5 to 1.0 cc. of one of these bronchodilator agents nebulized continuously with oxygen or with the simple Eliot air-pump unit made by the National Cylinder Gas Division of the Chemetron Corp. This treatment generally requires 10 to 15 minutes at a flow rate of four liters per minute.

Aminophylline.—Patients vary in their tolerance to aminophylline. Some become more alert; others become drowsy; many become nauseated and even vomit; and still others complain of palpitation and sweating.

Oral Route: For the prevention of mild but chronic attacks of bronchoconstriction, aminophylline may be given orally, around the clock. The addition of antinausea factors (local and central acting) to aminophylline has made possible the oral administration of larger, effective doses, with or without the addition of ephedrine, iodides, or a barbiturate. A combined preparation containing 300 mg. of aminophylline, 150 mg. of aluminum hydroxide, and 30 mg. of ethyl aminobenzoate (Cardalin), or a preparation containing 200 or 250 mg. of aminophylline, with 15 mg. of ephedrine hydrochloride or 25 mg. of phenobarbital and 15 or 30 mg. of pentobarbital sodium, 150 mg. of aluminum hydroxide, and 15 mg. of ethyl aminobenzoate (Dainite) is most helpful when the dose is carefully tailored for the individual patient's needs and tolerances.

Rectal Route: For more persistent attacks, aminophylline should be administered rectally in doses of 300 to 600 mg. in 15 cc. of tap water every 8 or 12 hours. For children, the dose may be reduced to 60 to 200 mg. The available suppositories are not of equal value.

Intravenous Route: Aminophylline should be given intravenously for severe paroxysms of coughing or wheezing not relieved by epinephrine or bronchodilator aerosols or by aminophylline given rectally. For an attack which has persisted for less than 12 hours, 250 mg. in 10 cc. of water for injection usually brings prompt relief. For a more protracted attack, the dose should be 500 mg. in 200 cc. of water for slow intravenous injection. These infusions may be repeated at intervals of 8 or 12 hours. Syncope and peripheral vascular collapse may be observed if the rate of injection is too rapid (1 cc. per minute is suggested).

For a severe acute attack of bronchial asthma occurring at home, which has failed to respond to self-administered bronchodilator aerosols, epinephrine, sedation, or oral forms of aminophylline, the following routine may be most helpful: 1. A dose of 500 mg. of aminophylline in 20 cc. of solution may be given intravenously. 2. If no lasting relief is ob-

served in half an hour, 0.2 cc. of epinephrine gel (Sus-Phrine) may be given subcutaneously. 3. If no lasting relief is observed in 15 minutes, 75 mg. of meperidine (Demerol) hydrochloride may be given subcutaneously.

If the patient has not previously used adrenergic agents, the order should be reversed to epinephrine gel, aminophylline, and meperidine hydrochloride. The attending physician should move quietly, yet act quickly, with assurance and empathy. The patient who does not respond satisfactorily in one hour's time would benefit most by proper hospitalization.

Continuous Infusion Technique: If intravenous injections of aminophylline become necessary one or more times daily for as long as a week, the continuous infusion technique should be employed. The patient should be hospitalized. A solution is made containing 500 mg. of aminophylline in each liter of 5% dextrose in water. Three liters should be given in 24 hours, with a flow rate of 30 drops per minute. If improvement follows after one or two days of such therapy, the infusions then may be given intermittently, e. g., from 9 a. m. to 9 p. m. daily, reducing the total to 1,500 cc. For the very sick patient, it may be necessary to continue these infusions for as long as 10 days. During convalescence, aminophylline should be given rectally instead of intravenously.

By means of pulmonary function studies, we have demonstrated the presence of latent bronchoconstriction in the patient who has completely recovered. Hence, in these patients, orally given aminophylline in combination with aluminum hydroxide and ethyl aminobenzoate should replace the rectally given aminophylline used during convalescence.

Intermittent Positive Pressure Breathing Therapy.—The use of pressure breathing is based on the creation of a pressure gradient from the mouth down to the pleural space. In the intermittent types, the gas mixture is supplied in the inspiratory cycle, usually through a face mask. There are several effective types of mask apparatus units which supply intermittent positive pressure breathing in inspiration. We have found the Bennett-type cycling valve and the new, extremely sensitive Mark 7 unit most satisfactory for administering positive pressure breathing, especially when combined with inspiratory bronchodilator aerosols. The patient completely controls the cycling of the valve by his own respiratory rhythm. An active inflation of the lungs occurs during inspiration under positive pressure from the cycling valve. The rapid release of pressure at the start of expiration is followed by a high velocity expiratory gas flow. This, combined with the release of bronchoconstriction which follows the simultaneous inhalation of bronchodilator aerosols, promotes better bronchial drainage. We employ pressures of 10 to 15 cm. H_2O with mixtures of air and oxygen. In general, this form of therapy should be reserved for the patient with chronic recurrent attacks who has some degree of complicating ventilatory insufficiency responsible for his disability. It is most useful in reeducation of diaphragmatic breathing and prevention of carbon dioxide retention. We have recently been able to demonstrate actual reduction in mechanical resistance and increase in pulmonary compliance, with resultant lowering of the work of breathing in these patients employing the Mark 7 unit.

In the presence of bronchial infection, bronchiectasis, or tenacious purulent secretions, the use of enzyme aerosols to attack the pus, such as pancreatic dornase (Dornavac), is indicated. It has proved to be efficacious in clearing bronchial infection of a chronic nature. Pancreatic dornase, dissolved in 0.5 or 1 cc. of the bronchodilator aerosol, is administered by aerosol in doses of 50,000 to 100,000 units, one to three times daily for five to seven days, with the continuous aerosol technique or with intermittent positive pressure breathing. It is used in addition to, not instead of, antimicrobial therapy.

Therapeutic Gases.—Oxygen Therapy: If there is hypoxia and cyanosis, the patient should be given oxygen. His physical and personal requirements, as well as the concentration of oxygen desired, should be considered in selecting the type of equipment to be used. Unfortunately, most patients in status asthmaticus tolerate poorly the tight-fitting rubber face masks which are necessary when concentrations of oxygen above 60% are indicated. The simple Eliot plastic face tent supplies average concentrations of 50% oxygen in the inspired air, with oxygen flow rates of six liters per minute. The patients do not complain of claustrophobia or a sense of suffocation.

In general, there has been an overemphasis on the danger of inducing the carbon dioxide intoxication syndrome and respiratory acidosis by the sudden administration of high concentrations of oxygen in patients with classic intractable bronchial asthma. This danger, however, is always present in patients with chronic hypoxia secondary to chronic pulmonary emphysema or chronic pulmonary heart disease, particularly if respiratory depressing drugs are administered before, or along with, the high concentration of oxygen. In these patients the plastic nasal cannula-humidification technique is best employed. Initial low concentrations with flow rates of one liter per minute should be used. The flow rates may be cautiously increased by daily increments to six liters per minute, and subsequently the therapy may be maintained more simply and safely with the Eliot plastic face tent.

Helium-Oxygen Positive Pressure Breathing: If obstructive phenomena predominate, mixtures of 75% helium and 25% oxygen are more beneficial than oxygen alone. Subjective relief of dyspnea and

wheezing may be observed frequently after positive pressure breathing of helium-oxygen mixtures. The gas mixture may be administered through the metered mask apparatus (made by the National Cylinder Gas Division of the Chemetron Corp. or by the Oxygen Equipment Manufacturing Corporation) which supplies an expiratory positive pressure when the exhaled air passes through constricted orifices. This method may be tiring, and the patient should be treated for periods of one-half to one hour four times daily. Rebreathing from the collecting bag may be permitted as an economy measure (helium saving). The intermittent positive pressure breathing unit may be employed; it is most efficacious and less tiring for the patient but more costly.

Bronchial Evacuation ("Catharsis").—The bronchitic cough is one of the most troublesome manifestations and may actually serve as the trigger mechanism for more extensive bronchiolar spasm. The therapeutic mechanisms for bronchial evacuation consist mainly in the use of (1) expectorants, (2) iodides, (3) ipecac, (4) positional drainage, and (5) bronchoscopy.

Expectorants: The expectorant drugs may prove quite helpful when properly used. A patient with an effective productive cough should not be oversedated, or the mucus in the bronchioles may become tenacious and inspissated, largely from dehydration and long retention. If the mucus is permitted to become impacted, the cough may become ineffective, and a state of "tussive insufficiency" will develop. One of the antihistamine preparations, a combination of diphenhydramine hydrochloride and aminophylline (Hydryllin) may be of value, particularly in patients with associated vasomotor rhinitis. Among the more ideal expectorants are the iodides, ipecac, and aerosols of water or detergents such as superinone (Alevaire) and Tergitol 08.

Iodides: Iodides are excellent bronchial evacuants. In the very sick patient, 1 to 2 Gm. of sodium iodide may be added to each liter of infusion fluid and administered for several days. When effective productive coughing occurs, the iodides may then be given orally again. Their action results in dilution and liquefaction of the retained secretions. Iodides are more efficacious when the patient is well hydrated. A disagreeable metallic, bitter taste is commonly experienced. The usual precautions in the use of iodides should be observed; namely, close watch for evidence of a variety of rashes and swelling, conjunctivitis, coryza, bronchorrhea, thyroiditis, and adenopathy. Administration should proceed cautiously. The initial dose should be 0.2 cc. of the saturated solution of potassium iodide after each meal and at bedtime. This may be increased by 0.1 cc. per dose each day until a maximum dose of 1.3 cc. is reached. The dose should then be abruptly reduced to 0.2 cc. and the same gradual increase of dosage repeated; this may prevent the development of intolerance. For patients in whom gastric irritation develops from a saturated solution of potassium iodide, enteric-coated tablets are available in 500 mg. and 1 Gm. sizes.

Ipecac: Ipecac acts by substituting effective retching in the place of ineffective coughing. Syrup of ipecac may be administered in doses of two or three teaspoonfuls followed by a cup of lukewarm boiled water. This dose may be repeated several days later, if indicated. It is always worth a trial before bronchoscopy is attempted.

Positional Drainage: Although of little benefit to those with useless cough, positional drainage may be of considerable value to the patient with accumulated secretions that are easily raised. The procedure is generally most efficacious in the management of associated bronchiectasis. It is more effective when carried out after bronchodilator therapy.

Bronchoscopy: One of the most common and important causes of death in asthma is obstruction of the larger and smaller air passages by inspissation of tenacious secretions. At times, spectacular improvement may follow bronchoscopic aspirations, even in a moribund patient. Because of the danger of serious reactions to the use of tetracaine hydrochloride or cocaine sprays and instillations for local anesthesia in asthmatic subjects, we generally prefer deep surgical anesthesia with ether. Intensive bronchoscopic aspiration is followed by marked subjective and objective improvement. It may prevent atelectatic complications, prove lifesaving, and be followed by a long period of remission.

Antitussive Measures.—The most effective antitussive measures center about the prevention of various trigger mechanisms responsible for the coughing paroxysms. Laughter, shouting, talking, crying, inhalation of tobacco smoke, dusts, fumes, fogs, and smogs, sudden changes in temperature and humidity, and exertion are among the leading causes in precipitating troublesome coughing paroxysms, which frequently induce bronchospastic crises, expiratory ball valving, and actual alveolar disintegration. The patient should always be on the alert for these causes, and the sooner he learns his tolerance to these factors the more successful the "cure."

In a recent study in our laboratory we found that benzonatate (Tessalon) was a most helpful agent in the management of pharyngitis and tracheobronchitis. Administered as an aerosol or syrup sipped slowly, this preparation has a pleasing surface-anesthetic effect which, though short-lived, is free of the side-reactions observed with the "caine" preparations. When given orally (in the form of perles), there is suggestive evidence that the antitussive effect occurs by action at the pulmonary parenchymal proprioceptor centers. For more sustained effects in the patient with intractable coughing paroxysms during the daytime, intensive therapy

with noscapine (Nectadon), 30 to 60 mg. given orally at graded intervals, has proved quite beneficial. We have not observed respiratory depression, significant drowsiness, or constipation with its repeated use. At bedtime, 15 to 30 mg. of dihydrocodeinone bitartrate has been most beneficial in suppressing the severe nocturnal coughing paroxysms.

Sedation.—Anxiety, fear, insecurity, restlessness, nervousness, insomnia, and mood and personality deviations are commonly encountered in patients with chronic recurrent attacks. These symptoms and a frank "alert state" may be accentuated by the very medications that these patients require, namely, aminophylline, adrenergic compounds, and the corticosteroids.

Heavy sedation should be avoided and only agents with a wide margin of safety used. Sodium bromide or chloral hydrate are helpful for the patient with mild, chronic recurrent attacks. When an attack has persisted for more than several hours, sedation should be given in addition to epinephrine and aminophylline given intravenously.

Meperidine hydrochloride, used in proper dosage, is a useful and safe drug in the treatment of the patient in an acute asthmatic attack or in status asthmaticus when the usual methods of treatment have failed or when fastness to epinephrine or aminophylline has developed. It has a far wider range of safety than morphine. The use of meperidine for a total of two to five days, administered at intervals of six to eight hours orally or parenterally in doses of 50 to 100 mg., has not caused addiction in our patients, even when this course was repeated at intervals of several weeks. However, we do not recommend its routine use in any of these patients. Meperidine can, of course, depress respiration if given in too large a dose or if repeated too frequently in patients with chronic bronchial asthma and associated emphysema.

If meperidine is contraindicated or not well tolerated, a retention enema of paraldehyde (20 to 30 cc.) or ether (60 to 70 cc.) may be administered at intervals of six or eight hours. These have proved of particular value in seriously ill asthmatic patients. Unfortunately, they are often irritating and difficult to retain.

Chlorpromazine (Thorazine), prochlorperazine (Compazine), and meprobamate (Equanil, Meprospan, Miltown) or similar "tranquilizers" may be of considerable clinical value in allaying the anxieties of seriously ill patients. In the hospitalized patient, 50 mg. of chlorpromazine hydrochloride may be administered intramuscularly upon admission and at eight-hour intervals for two to four days. Many patients with marked mood swings, anxiety, and compulsive behavior patterns receive considerable benefit from carefully selected, relatively nontoxic "tranquilizers" when administered over periods of many months. The pepped-up reactions and mood swings noted secondary to corticosteroid therapy have also been allayed in many patients with the simple addition of meprobamate plus prednisolone (Meprolone).

Management of Infections.—Evidence of respiratory tract infection is present in most patients with intractable bronchial asthma. Study of the sputum usually reveals polymorphonuclear leukocytes, bacteria, or pus in these patients. The leukocyte count, polymorphonuclear counts, and sedimentation rate may also be elevated. In general, the choice of the antimicrobial agent depends upon the predominating organisms, their drug susceptibility, and the patient's tolerance for the drug itself. Perceptive clinical judgment, tempered by practical bacteriological observations, is necessary in deciding what drugs or combination of drugs and dosages should be employed in an attempt to suppress the total infection. Complete eradication occurs rarely.

Although the clinical activity of penicillin is entirely confined to infections caused by gram-positive micro-organisms, it is the most useful agent in these patients. Unfortunately, the high incidence of local or generalized allergic reactions to penicillin aerosol in these patients limits this technique, which is otherwise most useful for the management of chronic bronchial infections. Penicillin is of particular value for hemolytic streptococci, since one does not usually encounter resistance. Unfortunately, an increasing number of strains of hemolytic staphylococci are penicillin-resistant. In these instances, erythromycin (Ilotycin), novobiocin (Albamycin, Cathomycin), kanamycin (Kantrex) sulfate, or chloramphenicol (Chloromycetin) should be administered. Because of the finding of mixed gram-positive and gram-negative organisms in most of our hospitalized patients seriously ill with intractable bronchial asthma and respiratory tract infections, we have administered combinations of 300,000 units of procaine penicillin G and 500 mg. of streptomycin sulfate every 12 hours. These combinations should be employed only for three to seven days because of the development of resistance to streptomycin in numerous instances. The incidence of severe reactions to penicillin given parenterally in patients with chronic bronchial asthma is higher than in the general hospital population, and a careful history of previous experiences with this drug should be elicited.

As an alternative or as a primary choice, one of the broad-spectrum antimicrobial agents—oxytetracycline (Terramycin), chlortetracycline (Aureomycin), tetracycline (Achromycin, Panmycin, Polycycline, Tetracyn), or chloramphenicol—may be used. In seriously ill patients, dosages of 250 mg., administered at six-hour intervals during the meal or with a glass of milk, may be employed for several days. The dosages should be tapered downward as soon as possible. Evidence of proctitis, Monilia invaders, granulocytopenia (with use of

chloramphenicol), complicating Proteus vulgaris organisms, pseudomonas infections, and idiosyncrasy should always be looked for. The addition of nystatin (Mycostatin) when fungi appear in the sputum is advisable.

Confronted with the problem of an overwhelming bilateral pneumonia in a patient with intractable bronchial asthma which is not responsive to a host of antimicrobial agents, the physician is justified in adding corticotropin (Acth, Acthar, Corticotropin) or soluble hydrocortisone sodium succinate (Solu-Cortef).

Prophylactic antimicrobial therapy is of considerable value in debilitated patients with intractable bronchitis and asthma who are subject to recurrent respiratory tract infections during the winter months. In general, we employ orally one of the following antibiotics in the stated dosages: 500 mg. of sulfadiazine, 100,000 units of penicillin, or 100 mg. of tetracycline, given every 12 hours. These doses occasionally require slight revision.

It should always be kept in mind that to suppress or eradicate bronchial infection it is not sufficient to convert a purulent sputum to a mucoid one. The sputum must be adequately evacuated by employing the aforementioned principles of bronchial evacuation, with the use of positional drainage, expectorants, bronchodilator aerosols, pressure breathing therapy, and bronchoscopy.

An irreparable sinobronchitic syndrome often follows in the wake of chronic paranasal sinus disease. Free drainage of the paranasal sinuses and elimination of infection should be attempted. Allergy appears to be the dominant factor in most patients. The topical use of the "safer" vasoconstrictor drugs, such as phenylephrine hydrochloride in combination with an antihistaminic, corticosteroid, and antibiotic agent, is of considerable aid in maintaining nasal patency and limiting infection. With evidence of frank purulent infection, 100,000 units of potassium or sodium penicillin G may be added to 1 cc. of 1% phenylephrine hydrochloride and administered with the Eliot air pump unit employing nebulizer and nasal tips. Treatments can be given at intervals of four to six hours for days or weeks, as indicated and tolerated.

Remissive Measures.—The use of adrenal steroid therapy should represent but a single phase, albeit important, in the total therapeutic program. Although these hormones frequently have a striking ameliorative, anti-inflammatory, and antiallergic clinical effect (antiphlogistic), they seem only to arrest the disease and usually do not suppress it. They should be employed for restricted and considered use when all other conventional methods of therapy have proved ineffective in securing a remission. Unfortunately, in the management of the patient with chronic bronchial asthma, the physician pushing steroid therapy may find himself like the man holding the tiger's tail because of the problems attendant to withdrawal therapy.

Changes During and After Hormone Therapy: Accumulation of eight years' clinical experience and extensive laboratory studies with these hormones have resulted in recognition of the many side-effects and toxic reactions as well as an appreciation of the precautions and contraindications to be observed. The undesirable effects that may follow the clinical use of hormones may be classified generally into two groups, those caused by overdosage and those caused by withdrawal of the hormone. Since successful steroid therapy depends upon a state of hormone overdosage, it is unavoidable that effective hormone therapy will be associated with an exaggeration of the patient's normal physiological actions. Any of the symptoms and finally the full-blown picture of adrenocortical hyperfunction (Cushing's syndrome) may develop. In particular, diabetes mellitus, gastrointestinal hemorrhage, hypertension, osteoporosis, and growth arrest in children should be closely watched for.

Symptoms of hormone withdrawal are the result of a state of adrenal insufficiency created by hormonal suppression of adrenocortical function. The symptoms may be mild or severe, depending upon the dosages employed, duration of therapy, and rate of withdrawal of the hormone. This state of relative adrenal insufficiency may resemble the course of adrenal cortical hypofunction (Addison's disease). Any additional stress in the form of trauma, shock, surgery, or severe infection during this state of insufficiency may prove disastrous to the patient.

On decreasing the dose during withdrawal of the hormones, aches and pains, lassitude, and a wide spectrum of personality changes may occur. These symptoms usually clear up when the dose is increased but may recur when another attempt is made to decrease the dose. A delicate balance must be found with each patient.

The wide varieties of changes noted during and subsequent to steroid therapy are listed as follows. The less serious changes include facial mooning, acne, petechiae, purpura, edema, hirsutism, skin pigmentation, increased appetite, insomnia, headaches, aches, pains, weakness, lassitude, euphoria to mild depression, mental and physical hyperactivity, hypertension, tachycardia, glycosuria, hyperglycemia, aggravation of existing diabetes, depressed thyroid function, thrombophlebitis, and sensitivity reactions to corticotropin given intramuscularly, such as skin rashes, pruritus, urticaria, occasional wheezing, and angioneurotic edema. The more serious changes include potassium deficiency, muscular weakness, negative nitrogen balance, osteoporosis and fractures, especially in women after menopause and in immobilized patients, masked infections (bacterial, viral, and fungal), spread of

existing infections, serious spread of nonpathogenic inhabitants of the gastrointestinal and respiratory tracts, mental confusion to severe psychotic manifestations, convulsions, exacerbation of quiescent ulcers, gastrointestinal hemorrhage and perforation, activation and spread of unsuspected or inactive tuberculosis, sensitivity reaction (anaphylactic shock), periarteritis, and postoperative adrenal insufficiency. The most serious or fatal changes include the withdrawal syndrome, "adrenocortical storm," poor tolerance to trauma, shock, and infections, and active atrophy of adrenal cortices.

Therapeutic Precautions: Among the therapeutic precautions to be followed are restriction of sodium chloride in the diet to 750 mg. daily, with corticotropin, cortisone (Cortisone, Cortogen, Cortone) acetate and hydrocortisone (Cortef, Cortril, Hycortole, Hydrocortone) therapy. The newer corticoid analogues do not usually require this strict restriction. The occasional use of chlorothiazide (Diuril) may be helpful when indicated by the presence of hypertension and/or the excessive weight gain from fluid and salt retention. Potassium may be routinely administered in the form of a tableted mixture containing 500 mg. of ammonium chloride and 500 mg. of potassium chloride (Pot-Amide), 8 tablets daily. Supplemental potassium in the form of orange or cranberry juice (8 to 12 oz. daily) is preferred by many patients. The supplementary ammonium chloride in the Pot-Amide preparation acts as a mild diuretic agent and is followed by excretion of sodium and water. Potassium replacement is best carried out when the salt-retaining type of steroids is employed. This is of particular value in patients with moon-face, fluid and salt retention, and weight gain syndrome. In the presence of infection or suspected infection, the concomitant use of an antimicrobial is advisable. In general, the patient should receive a high-protein diet to offset the tendency toward negative nitrogen balance. For patients with a tendency toward gastric hyperacidity, it is advisable to prescribe antacids and belladonna alkaloids during hormone therapy. Periodic guaiac tests of finger specimens of stool are advisable in these patients and in others suspected of having gastrointestinal ulceration. When in doubt, a series of x-rays should be taken as a control measure. The use of androgens and/or estrogens is perhaps indicated when the patient receiving hormone therapy has evidence of osteoporosis, noted more usually in patients over 50 years of age who are on long-term therapy. Patients should receive adequate supplemental doses of corticosteroids in case of surgery, severe trauma, or other forms of major stress. To minimize adrenal suppression and atrophy in patients receiving long-term therapy with the corticoids, corticotropin gel may be administered periodically, and particularly when corticoid withdrawal is started.

Hormones.—Hormonal therapy should not be used until all of the other measures which may be indicated have been adequately employed. Finally, hormonal therapy is best employed in conjunction with the foregoing measures to secure a more effective and lasting remission, with the lowest possible dosage schedule and freedom from side-reactions. In patients with severe seasonal (pollen) asthma, short-term therapy should be administered when the patient has failed to respond within a week to intensive antihistaminic and bronchodilator therapy started at the very outset of symptoms.

Oral Route: The following corticosteroids have been used orally in order of their development: cortisone, hydrocortisone, prednisone (Deltasone, Deltra, Meticorten), prednisolone (Delta Cortef, Hydeltra, Meticortelone), methylprednisolone (Medrol), triamcinolone (Aristocort, Kenacort), and more recently, dexamethasone (Decadron, Deronil). In general, it has been our custom to consistently employ lower initial therapeutic and maintenance dosages and to withdraw the drug with smaller reductions and over a longer period of time than reported by other investigators. This is possible when intensive supplemental, physiologically directed therapy is carried out simultaneously. It is our belief that fewer significant side-reactions will then be observed. Nevertheless, a continuous high index of suspicion of the hazards previously listed must be maintained at all times. This applies to all corticoid analogues, regardless of their purported safety features.

We have observed considerable variations in individual responses to the steroids. On occasion, a patient not responsive to prednisolone has shown dramatic improvement with cortisone or hydrocortisone. Similar observations may be noted with the newer prednisolone analogues triamcinolone and dexamethasone. The physician should be prepared to change preparations from time to time. The advantages of less profound alteration in potassium depletion and sodium retention, in the face of adequate anti-inflammatory properties, and the ability to select the agent best suited for the individual patient's appetite needs have given these newer corticoid analogues a more desirable status for general use than the parent compounds, cortisone and hydrocortisone.

During the seasonal (pollen) bouts of bronchial asthma, steroid therapy should be employed on a short-term basis only when the more conservative physiological measures have failed. Therapy over the shortest period of time commensurate with the patient's pollen season is usually adequate. The patient with tree, grass, and ragweed pollen asthma may not require therapy during the entire period from spring to Labor Day. Individual variations in sensitivity to different pollens may be elicited in careful history taking of previous years. The patient with ragweed pollen asthma is particularly grateful.

For the patient with chronic, intractable bronchial asthma, when vigorous therapy has failed, long-term steroid therapy becomes necessary. The physician does well to be "reluctantly forced into therapy" rather than to start it at once. He should not be motivated by the desire to show the patient, his family, and friends a brilliant therapeutic result by first starting steroid therapy.

During the past three years we have observed the effects of prednisolone in more than 400 adult patients with various types of chronic bronchial asthma and associated allergies. The dosage schedule most commonly followed was 5 mg. four times daily for the first three days, 5 mg. three times daily for four days, 5 mg. twice daily for seven days, and 5 mg. or less daily thereafter. Approximately 10% of the patients were able to remain on maintenance doses of 2.5 mg. Another 10% required slightly higher revisions initially and for maintenance. The majority of the patients were maintained on 5 mg. daily. During periods of unexplained stress or infections, the patients were permitted to return to their initial starting schedule, followed by the same gradual reduction. The reduction in dosage for withdrawal from long-term therapy is presently advised at 1 mg. per month. The drug may ultimately be spaced at intervals of two or three days during withdrawal. Preparation for surgical procedures is accomplished by returning to the full initial schedule two days before surgery. At times, supplemental hydrocortisone sodium succinate therapy given intravenously on the day of and after surgery is advisable.

With the use of prednisolone-meprobamate, we have not observed any over-all reduction in the basic dosage requirements. However, many patients with steroid-alert manifestations and patients during the pollen season appear to prefer this combination. It was considered best to maintain patients, with a past history of gastrointestinal bleeding, on buffered prednisolone (Co-Hydeltra). Supplemental antacid therapy is often advisable.

We recently reported on our observations in 44 patients with chronic bronchial asthma and allied disorders who were treated with triamcinolone. An additional 32 patients with chronic bronchial asthma have been studied since this report. There appeared to be a greater weight loss in this series than in the series who were given prednisolone. The over-all results were good; facial mooning and weight gain in some patients, but no serious sequelae, were observed. We have not observed any anorexia, weakness, or clinical evidence of excessive nitrogen or potassium loss in our patients with chronic bronchial asthma. The dosage requirements were on the order of 4 mg. of triamcinolone to 5 mg. of prednisolone (4:5). The schedules previously described for prednisolone were followed.

At the present time, we have under observation 52 patients with intractable bronchial asthma being treated with dexamethasone. This is an unusually interesting new steroid agent; more than one-half of the patients have noted tremendous increase in appetite and consistent weight gain. The weight gain has been influenced but little with supplemental chlorothiazide. However, there appears to be a greater incidence of bleeding from the gastrointestinal tract thus far in our observations. Two patients developed bleeding; one had no history of peptic ulcer, whereas the other gave a history of duodenal ulcer. Dexamethasone appears better suited for the debilitated patient in whom weight gain is important. The dosage of this agent required for suppression of asthma is in the ratio of 1:3, as compared with that of triamcinolone.

Intravenous Route: The intravenous route is more efficacious for the hospitalized patient in serious status asthmaticus. The patient is started on a continuous infusion of 5% dextrose injection, 30 drops per minute flow, thus ensuring approximately three liters per 24 hours. Aminophylline, 250 to 500 mg., is added to each liter, depending upon the patient's responses and tolerance. For the patient who has not received steroid therapy recently, 10 mg. of corticotropin is added to each liter, and a total dose of 30 mg. per 24 hours is given for one to three days. Those who have been on corticosteroids should receive hydrocortisone or hydrocortisone sodium succinate given intravenously. The quantitative eosinophils, which are consistently elevated at the outset, are usually low or absent by the second day of this program. With improvement in the patient, the corticotropin is administered only in the first liter of fluid daily for several more days. In the most severe cases, the infusion of dextrose and aminophylline is continued for an additional one or more days. With intravenous therapy the immediate results are generally more striking. However, the physiological hazards, particularly disturbances in psyche, potassium imbalance, and facial mooning, may be more pronounced.

Attempts should be made to maintain the remissive state with the use of aminophylline solution given rectally or oral preparations of aminophylline and bronchodilator sprays, given as needed. During treatment and after remission, many patients note that they can "do more with considerably less" of their therapeutic armamentarium.

Surgical Management

The proper management of the patient with chronic recurring bronchial asthma may tax the character and ingenuity of the physician. The therapeutic problem may be made even more difficult by the family and the disturbed emotional make-up of the patient. The physician should ac-

quire a proper attitude of empathy rather than overt sympathy, and he should strive to firmly adjust the patient's personality to his disease. A mutuality of confidence must be established. Every severe asthmatic episode should be carefully considered apart from previous seizures. The "whims and cure-alls" of his patient and family should not be curtly dismissed but discussed rationally.

Unfortunately, too often, as with many chronic diseases, the hope of "surgical cures" is brought up. Benefit has been described after a wide variety of surgical procedures, and, indeed, specificity has been "suggested" for these measures. Notwithstanding the great technical skill of the modern thoracic surgical team, there appears but little enthusiasm for the operative procedures designed for the purpose of influencing the neurogenic control of the bronchioles and chemical secretions. Unfortunately, observations made in the laboratory on cats and dogs cannot be translated accurately into changes to be observed in humans with chronic bronchial asthma. Occasionally, brilliant temporary results have been reported after procedures attacking the sympathetic or parasympathetic (vagal) or both systems. These procedures have varied from the simpler procedures designed to block vagal influences, such as procaine injection to the vagal fibers in the mastoid region and procaine or alcohol block of the sympathetic stellate ganglions and the upper four thoracic ganglions, through a variety of unilateral and bilateral cervicothoracic sympatholytic or parasympatholytic designed resections. Finally, bilateral resection (two stages) of the posterior pulmonary plexus as well as resection of cervicothoracic sympathetic and complete pulmonary plexectomies have been performed. No unanimity of opinion as to the ideal surgical procedure for these hapless patients can be found. In fact, most of the early enthusiastic surgical investigators have stopped their search for surgical surcease. Many patients improve temporarily after these procedures. Long periods of rest in the hospital and intensive medical care may well explain this. The physiological and financial stress of major surgery, the attendant pain and discomfort, the complications of pneumothorax with ganglion surgery, trauma to bronchi and blood supply, with intrathoracic procedures and the discomfort of residual, unilateral, or bilateral Horner's syndrome and skin temperature changes noted after sympathetic surgery (the patient "looking and acting like a sad St. Bernard Dog") are quite disconcerting to say the least.

There is still another surgical procedure which has found some favor among thoracic surgeons. Beneficial results have been described in patients in whom excision of "trigger areas" of pulmonary destruction (bronchiectasis) or excision of areas of large emphysematous bullae was carried out. Excisional surgery, along with some type of interruption of the upper sympathetic or parasympathetic vagal chain below the level of the recurrent laryngeal nerve, is usually advocated by these surgeons. Definite bronchiectatic disease (saccular), which is unequivocally demonstrable (after maximal bronchodilation) by radiography and bronchography and which has served as a nidus for recurring pneumonitis, chronic suppurative disease, pulmonary hemorrhage, or progressive debility, should be dealt with as bronchiectasis per se and not as a possible "trigger mechanism" for chronic bronchial asthma. The indications for resectional surgery in these patients are clear-cut and uniformly accepted, and the curative results from the effects of the bronchiectasis are excellent. However, the course of the associated chronic bronchial asthma is usually not affected for long. The segmental bronchial areas, suggesting cylindrical bronchiectasis by radiography or bronchography, should not be resected unless the well-defined criteria referred to previously for resection of a proved saccular bronchiectatic area are present. After resection, lasting improvement should not be expected in the associated chronic bronchial asthma.

Similar criteria should be applied to the patient with chronic bronchial asthma, secondary chronic pulmonary emphysema, and large bullae (seldom seen in this order of relationship). Demonstration of a progressive space-occupying lesion, which is encroaching on functioning lung, an expiratory check-valve mechanism, and repeated bronchopulmonary infections with laboratory evidence of ventilatory insufficiency despite adequate therapy, is an indication for surgical intervention in patients with large bullae associated with chronic pulmonary emphysema and secondary bronchospastic crises. The choice of plication, excisional procedure, or another type of tailoring operation should be individualized.

The author has a dim view of the present status of the aforementioned thoracic surgical procedures for the cure or amelioration of chronic bronchial asthma. After surgery these patients generally continue to require long-term intensive medical therapy. Fortunately, physical rehabilitation and the use of adrenal steroid therapy, particularly with the newer corticoid analogues with potentially less mineralocorticoid reactions, intensive bronchodilation, and antibiotic therapy, have made their care more pleasant. Nevertheless, more adequate management of this large group of "pulmonary cripples" continues to remain a challenge to the family physician and the specialist. Unfortunately, these patients all too frequently require an "economic prescription."

The dexamethasone used in this study was supplied as Decadron by Dr. Elmer Alpert of Merck, Sharp & Dohme Research Laboratories, Division of Merck & Co., Inc., Rahway, N. J.

COUNCIL ON INDUSTRIAL HEALTH

THE LEGAL SCOPE OF INDUSTRIAL NURSING PRACTICE

This report has been prepared by the Committee on Industrial Nursing of the Council on Industrial Health, American Medical Association, in collaboration with the Association's Legal Division.

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The purpose of this report is to discuss the legal scope of the practice of industrial nursing and the functions which a professional industrial nurse may legally perform. The intensification of the educational program of nursing, the increased dependence of the physician on the skills and discretion of the nurse, and the ability of the nurse to meet the challenge of an ever-rising standard of patient care have motivated the nursing profession to define and seek recognition for those professional functions which the nurse performs independently. This is especially true of the industrial nurse who often works without immediate medical supervision.

The Practice of Nursing

Nursing and medical practice are interrelated and frequently indistinguishable from each other. The same act may be clearly the practice of medicine when performed by a physician and likewise a practice of nursing, depending on the circumstances, when performed by a nurse.

There are, of course, limitations on the functions which the nurse may perform, whether independently or under the supervision of a physician, and there are likewise limitations on the functions which may be legally assigned by a physician to a nurse. These will be discussed in this report.

The statutes of the various states which define professional nursing are too nebulous to provide a usable guide in determining the functions in which a nurse may legally engage. Essentially the statutes define professional nursing as involving the carrying out of treatment prescribed by a licensed physician and the application of nursing skills. Obviously, such definitions do not identify the particular functions in which a professional nurse may engage.

Probably the lawmakers should be commended for their foresight rather than criticized for ambiguity. A half-century ago when the first nursing practice acts were adopted the principle function of the nurse was to aid the physician by performing tasks under his direction. The functions of nursing are constantly expanding, and precisely drawn statutory definitions of the functions of nursing could not be kept up to date with changes in professional practices. However, the growing body of judicial decisions reflects the development of the profession of nursing and its expanding responsibilities in the wake of medical progress. The identification of particular functions as nursing functions and the standards of competence required of professional nurses in executing these functions have undergone a rapid and continuous process of evolution among those who are professionally responsible for the care of the sick and injured.

Courts have held that professional nurses have a legal duty to interpret evidence presented by the patient possibly indicating the need for medical attention, and to proceed in the light of that interpretation to do what is required for the patient, as for example the need to call a physician [1]; to discontinue a treatment where there is evidence of its harmful effect, e. g., on an unconscious patient [2]; or to determine the patient's need for special medication, e. g., sedatives.[3] There can be little doubt that by custom and usage the relationship between doctor, patient, and nurse is one in which the parties recognize that the nurse as well as the physician has the function and responsibility to observe and interpret the patient's reactions.

The observation of symptoms and the making of a diagnosis imply the need for professional learning and mental acuteness. These functions are characteristic of the professional nature of nursing as well as medicine. The industrial nurse who observes the extent of illness or injury to an injured workman and determines whether she should render emergency treatment or wait until the physician arrives has made a vital diagnosis comparable in importance to many of those which physicians are called on to make. However, except for first-aid treatment and the employment of such measures as will prevent aggravation of the patient's

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injury or illness, the determination of therapy is within the exclusive domain of medical practice and beyond the limits of nursing practice.

Nurse's Malpractice

In *Cooper v. National Motor Bearing Co.*[4] the defendant appealed from a judgment in favor of the plaintiff in a malpractice action brought against a registered nurse and her employer.

In May, 1951, the plaintiff received a puncture wound on his forehead when another employee let a piece of metal slip from his hand. He went directly to the first-aid room and received treatment from the defendant nurse. She swabbed the wound with an antiseptic and put a bandage on it. According to the plaintiff's testimony she did not examine or probe the wound. He was told to return the next day which he did. The nurse again applied antiseptic but did not probe the wound. On the next day he also went to the dispensary, but on that occasion the nurse just looked at the wound.

On visits to the dispensary over a period of several months the plaintiff would point out to the nurse that the wound did not seem to be healing properly and she would say that if it did not she would have to do something. In March, 1952, the plaintiff visited the dispensary for a check of a chest injury and asked the nurse if she would send him to a doctor to examine his forehead. She referred him to a physician who excised a piece of tissue for laboratory examination. A pathologist examined the specimen and reported that it contained a basal cell carcinoma. On March 23, 1952, the plaintiff was operated on and a larger area was excised. Skin was removed from his right forearm and grafted to the forehead.

The plaintiff's case was tried on the theory that a metal splinter was left in the wound by the negligence of the nurse and that this foreign body, acting as an irritant, caused the cancer.

The nurse admitted that it was her duty to refer any condition or injury she was not familiar with, or sure about, to a doctor for diagnosis. The standard of good nursing care in the community required the nurse to examine the wound for foreign bodies. If splinters were too deeply embedded, the nurse was to send the workman to the doctor. The plaintiff's type of wound should normally have healed in about a week. If a wound persisted and did not heal, proper nursing care would require that the workman be sent to the doctor. The nurse admitted that she was familiar with the danger signals of cancer, one of which is "any sore that does not heal." Nevertheless she continued to treat the wound for 10 months before sending the plaintiff to the doctor.

In affirming the judgment of the trial court, the California District Court of Appeal said:

> a nurse's diagnosis of a condition must meet the standard of learning, skill and care, to which nurses practicing that profession in the community are held. A nurse in order to administer first aid properly and effectively must make a sufficient diagnosis to enable her to apply the appropriate remedy. Usually she receives some history of the accident or illness from the patient, inspects a wound, and bases her choice of treatment on the deductions thus made. She has been trained, but to a lesser degree than a physician, in the recognition of the symptoms of diseases and injuries. She should be able to diagnose, according to appellant nurse's own testimony herein, sufficiently to know whether it is a condition within her authority to treat as a first aid case or whether it bears danger signs that should warn her to send the patient to a physician . . .
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> Appellant nurse testified that it was the practice of a nurse in this type of industry to probe wounds for foreign bodies, that if there is a foreign body in a wound there is a feeling of sharpness on pressure, that according to the standard of care and her experience as a nurse, she should be aware of the possibility of foreign objects in such a wound.

If the plaintiff's cancer was the result of the nurse's failure to refer him to a physician for examination and treatment during the 10-month period during which she treated him, then it must be acknowledged that a judgment based on malpractice was proper. Employees as well as their employers are responsible for damages due to acts of negligence.

In other than emergency cases where a physician is not present, diagnosis is not a function of professional nursing and treatment by nurses is generally restricted to the execution of orders given by and under the direction or supervision of a physician. Furthermore, the nurse should only execute legally valid medical orders which she is qualified by training and experience to perform.

Nursing Functions

It is axiomatic that the practice of medicine may not be delegated to nonphysicians. Nevertheless there are numerous traditionally medical functions which are now also performed by nurses under the supervision or direction of a physician and recognized to be nursing functions. Accordingly, under the direction or supervision of a physician, a nurse may administer injections intravenously [5] or intramuscularly [6] or perform x-ray treatments.[7]

Basal metabolism tests, anticoagulant therapy, and the administration of blood transfusions and oxygen are now routinely performed by nurses. The great progress in the science of medicine has led to the delegation of numerous medical procedures to nurses. The first-aid equipment used by the industrial nurse today could have been used only by a physician not too many years ago.

On the other hand the order of a physician purporting to delegate to a nurse the authority to perform an abdominal operation, or an amputation, or to set a fracture or to perform any similar procedure would undoubtedly be considered invalid by the medical and nursing professions as well as the courts. In realistic terms, professional nursing prac-

tice includes not only emergency diagnosis and treatment but those medical acts and techniques which are commonly performed by qualified nurses under physicians' orders. Fundamentally, the scope of nursing practice is determined by medical custom. None of the statutes relating to nursing practice attempts to set forth the specific functions of nursing. This statutory flexibility has allowed for the rapid growth of nursing. Consequently the courts have been guided in identifying nursing functions by customs and practices of the medical profession, since physicians can best recognize the proficiency and attainments of nurses.

Emergency Treatment

A medical emergency may be defined as an unforeseen illness or injury which calls for immediate action for the safety of the patient.[8] Anyone, and not necessarily a professional nurse or a physician, may render first aid or perform medical acts to preserve life and limb in the case of an emergency. But one who renders aid in an emergency is under a legal duty to act as a reasonably prudent person. The qualified industrial nurse would generally be held to a greater degree of responsibility and skill than the layman, but to a lesser degree of responsibility than the physician.

Medical custom has permitted a broad definition of the term "emergency" to be applied. It ordinarily refers to situations requiring resuscitative or other first-aid measures. Guiding principles and procedures, approved by a responsible physician, are particularly useful to industrial nurses in such cases.

The case of *Burns v. Bakelite Corp.*[9] is a landmark court decision in the field of industrial nursing. It states the rule that an employer has a duty to provide emergency medical care and other assistance when an employee suffers a sudden illness while engaged in work. The court found that a registered nurse, acting on behalf of the employer, fulfilled this duty but many physicians and nurses may feel that the nursing profession is capable of maintaining a higher standard of performance than that demanded by this court. Because of its basic importance and interest, the holding and facts of the case are stated below in detail.

The plaintiff, who incidentally happened to be a trained nurse, alleged that the negligence of a registered nurse employed by the defendant was responsible for the death of her husband. The trial court judge before whom the case was tried took the case from the jury and rendered judgment himself for the defendant. In a jury case the trial judge is justified in doing this only "if fair-minded men could not differ" in their judgment.

The nurse, Mrs. B———, testified that on a certain morning the plaintiff, Burns, came to the dispensary, pale and perspiring, and she thought he looked ill. He complained of a severe chest pain and thought he had indigestion and he wanted peppermint for it. The nurse took his pulse and his temperature, and found both were normal. He had no difficulty in walking. The nurse suggested he see a doctor, but he refused to see the plant doctor whose office was only about two blocks away, and he asked for his own physician. The nurse tried unsuccessfully to reach the physician by telephone. Then the plaintiff asked her to send him home, and she summoned a car, a station wagon. Refusing assistance, he walked to the car and got in. By the removal of one of the station wagon seats, room could have been made for a stretcher, but the plaintiff was not put on a stretcher.

He was driven by the company's chauffeur to his home. The house was 50 ft. from the roadway, and to reach the front door it was necessary to mount seven steps. The chauffeur opened the door for the plaintiff and he got out and without aid walked to the house and climbed the stairs.

The nurse contacted the plaintiff's doctor soon after the plaintiff had left the plant but he was engaged in an operation and sent a colleague. The doctor gave a diagnosis of coronary occlusion. He was taken to a hospital where, six days later, he died. The opinion of the court states:

> Generally, no duty rests on an employer to provide medical service or care for an ill or injured employee. Yet when the employee, while engaged in the work of his master, suffers a sudden illness that renders him unable to provide for his own care, the employer must put in his reach such medical care and other assistance as the emergency thus created may in reason require. The duty arises out of necessity. . . .
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> The symptoms that the nurse observed were typical of the onset of a heart attack, although they might indicate acute indigestion or some other condition. But a physician would probably have made a tentative diagnosis of a "coronary occlusion" because that is the most common cause of such symptoms. Based on that diagnosis, the standard emergency treatment would have been the administration of morphine to relieve the pain, not only for the patient's immediate ease but because the pain causes reactions in the heart that increase the damage to that vital organ. And the patient should not be permitted to walk or to make avoidable physical effort. But Mrs. B——— is not a physician; she did not realize that Burns was suffering from a coronary thrombosis; she only knew he was ill and he did not appear to her to be seriously ill. Even if the nurse had made a diagnosis of heart attack, she was not authorized to administer morphine, for such drugs are administered only after the direction of a licensed physician. . . .
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> There is no negligence indicated by Mrs. B———'s failure to recognize the particular ailment from which Burns was suffering. But should the various symptoms that she observed and that we have recited have warned her it was dangerous to allow Burns to be taken home in the station wagon? If so, there was a failure to exercise due care. If fair-minded men, after carefully considering the facts, could differ in their answer, then the question should have been left to the jury. . . . Run over the facts again—face pale, perspiring, severe pain in chest, pulse and temperature normal, walked without difficulty; the man himself thought he had indigestion; the nurse thought he looked ill, but not very ill. In our opinion, there

was nothing to suggest that he was a stretcher case, or that there was need for other means than those employed, or for more care than was exercised in sending decedent home. We find no error in the award of judgment to defendant.

The significance of the case is that it recognizes the duty of the industrial nurse to make a tentative diagnosis of the patient's condition. The nurse was not held to the standards of diagnosis required of a physician, although the court felt that the symptoms were such that a physician would probably have made a tentative diagnosis of a heart attack. Actually, many industrial nurses would probably have suspected the symptoms in the case as common symptoms of a heart attack.

Summary

The profession of nursing is a dynamic discipline which embraces an ever-increasing number of functions. Nurses, particularly those employed in industry, should be careful to limit their diagnostic and therapeutic activities to emergencies and to avoid continued treatment of a patient unless such treatment involves the carrying out of the specific orders of a physician who is in charge of the case.

Under the direction or supervision of physicians, nurses are performing as nursing practice numerous procedures which were formerly performed exclusively by physicians. The limitations on the procedures which a nurse may properly perform are governed by (*a*) the nature of the relationship between the medical and nursing professions in the community, (*b*) the scope of training offered in recognized nurses' training schools, and (*c*) the training, experience, and proficiency of the individual nurse.

In emergency cases, industrial nurses have a duty to determine the need for prompt medical attention, to make a tentative diagnosis of the patient's condition, and to employ necessary resuscitative and first-aid measures.

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A PRUDENT WAY OF LIFE.—Perhaps Sir Thomas Lewis' description of a prudent way of life would not appeal to some of us, but its practice would no doubt be a forward step in the control of our nation's number one public health problem. "Very prudent people," said Lewis, "live quietly and moderately; they have their simple daily routine of work and pastime, enlivened by occasional excursions and entertainments, social gatherings and visits to and from their friends. They are temperate in their eating, taking no more than will maintain them in robust health, arranging their diet to consist chiefly of plain good food, relieved occasionally of its monotony by a more elaborate, but not heavy meal. They are regular in their habits of work and exercise, and in their mealtimes. They are strictly temperate in their drinking. They control their emotions and their passions. They avoid all forms of excess. They use tobacco little if at all. They welcome the freshness of abundant air and open spaces, delighting in the feelings of invigoration that accompany active exercise; they love the warmth of sunlight playing on their skins and the sleepiness of healthy fatigue. These are habits that few people in industrial countries now adopt, that fewer still maintain. The cares and distractions of an increasingly complex life, indoor or sedentary occupations, advancing years and the decreasing energy interfere less or more, and the prudent rules are neglected; neglect is the easier because the penalties, owing to the body's great power of resistance to disease, are uncertain in their incidence and often long deferred." Healthy habits would become more prevalent if the consequences of their neglect were more immediate and variable. Indeed, healthy habits, an optimistic philosophy, and the sound use of the abundant leisure which has made us the envy of the world, might well neutralize or retard the atherogenic mechanisms which are both initiated and accelerated by the "stress and strain" of our daily struggle for existence.—H. I. Russek, M.D., Emotional Stress and the Etiology of Coronary Artery Disease, editorial, *The American Journal of Cardiology*, August, 1958.

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AMMONIA TOXICITY AND HEPATIC COMA

HEPATIC COMA, characterized by a flapping tremor, disturbed consciousness, and electroencephalographic changes, may occur in patients with cirrhosis of the liver or with portacaval shunts.[1] It is generally believed that under such circumstances toxic substances absorbed from the intestine may escape the normal detoxification processes in the liver and hence enter the systemic circulation and reach the brain. The identity of the toxic agent (or agents) in hepatic coma has not been fully established, but considerable evidence has accrued to implicate ammonia in this respect. Ammonia is normally present in appreciable amounts in the portal vein, due to intestinal absorption of ammonia derived from the bacterial breakdown of nitrogenous foodstuffs. Ordinarily this ammonia, together with the endogenous ammonia arising from the deamination of amino acids, is converted to urea by the liver, but in the presence of liver disease, or if the liver is bypassed, appreciable amounts may enter the systemic circulation. Blood ammonia levels are usually elevated in hepatic coma and coma may be precipitated in susceptible persons by the administration of ammonium salts or urea or by other factors capable of elevating the blood ammonia level such as a high-protein diet or gastrointestinal hemorrhage.[2] Additionally, avoidance of nitrogenous foodstuffs,[3] alterations in intestinal flora by chemotherapeutic agents,[4] or the removal of blood ammonia by dialysis [5] may result in clinical improvement.

Despite the apparent association between ammonia toxicity and hepatic coma, it has repeatedly been observed that blood levels of ammonia do not always reflect the severity of the symptoms of hepatic coma or the development of electroencephalographic changes.[6] A possible explanation of such discrepancies has recently been advanced by Warren and his associates.[7] These investigators postulated that, since ammonia is a weak base and since weak acids and bases are known to penetrate the blood-brain barrier largely in un-ionized form, the cerebral toxicity of ammonia should be influenced by the pH of the blood. In substantiation of this, they injected a number of ammonium salts (chloride, acetate, bicarbonate, and carbonate) into mice and found that the toxicity of the salts increased in direct relation to their ability to increase the blood pH. Further, when the LD_{50} of the various ammonium salts was injected into the animals, the brain ammonia concentrations proved to be essentially the same for each salt although the blood concentration of ammonia varied directly with the dosage, thus indicating that the lethal effect of ammonia is cerebral in origin. It was concluded that as the blood pH was increased by the injected salt the amount of un-ionized ammonia (NH_3) was increased relative to that of the ionized (NH_4^+) form. Since the normal blood pH is quite close to the pK of ammonia, small shifts in blood pH could be expected to significantly affect this ratio of un-ionized to ionized ammonia and hence profoundly influence the degree of penetration of the blood-brain barrier by the ammonia. Indeed the data reported indicate that changes of pH in the order of 0.1 unit result in a 50% rise in the concentration of ammonia in the brain. Such a phenomenon would explain the recently reported association of coma and alkalosis in patients with elevated blood ammonia levels [8] and the increased tolerance to infused ammonium observed in dogs receiving 10% carbon dioxide.[9] It also suggests that acidifying agents may be valuable adjuncts in the treatment of hepatic coma and indicates the futility of attempting to correlate the degree of cerebral intoxication by ammonia by determination of blood ammonia levels without taking into account the blood pH.

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ORGANIZATION SECTION

REPORT OF THE COMMITTEE TO STUDY A. M. A. OBJECTIVES AND BASIC PROGRAMS

TO THE HOUSE OF DELEGATES AT THE CLINICAL SESSION, DEC. 2–5, 1958, MINNEAPOLIS

In our progress report to the House last June in San Francisco, we stated that our Committee was appointed by the Speaker pursuant to an action of the House in Philadelphia (December, 1957) modifying the recommendations of the Hyland Committee which earlier had been assigned the task of analyzing the report of the management consulting firm, Heller and Associates. Members of the House will recall that our Committee was requested to study four subjects: (*a*) redefinition of the central concept of A. M. A. objectives and basic programs; (*b*) placing more emphasis on scientific activities; (*c*) taking the lead in creating more cohesion among national medical societies; and (*d*) studying socioeconomic problems. This report sets forth our Committee's recommendations on these four topics.

At the conclusion of our report you will find the questionnaire and the two-page statement, "Genesis of the Committee," attached for your information. Inasmuch as all members of the House received the questionnaire, its inclusion here is merely for reference. Following the questionnaire itself are two long appendixes prepared for us by the Bureau of Medical Economic Research. Appendix A sets forth more than 1,600 quotations selected from the returned questionnaires. These actual words may mean as much to some members of the House as the statistical analysis of the returned questionnaires, which is the subject of Appendix B. In the latter, we would especially call your attention to the tests of the representativeness of the respondents to the questionnaire sent to a probability sample of physicians, members and nonmembers. These tests indicate that the respondents were so representative that replies from one or two thousand more respondents would probably have given the Committee very little additional information.

During our second meeting in San Francisco last June, the Committee reviewed progress on the survey, decided not to undertake a series of depth interviews, and made plans to terminate its investigation in order that the final report could be presented at the Minneapolis meeting. Our first meeting was held on March 15 of this year. The third meeting of the Committee was held in Chicago on Sept. 5 and 6 at which time this report was completed.

The historical background and appendixes to the report are available for study on a loan basis and may be secured by writing to the American Medical Association, Economic Research Department, 535 N. Dearborn St., Chicago 10.

Your Committee's report is based on many informal conversations by members of the Committee, personal correspondence, the 1,600 selected quotations (Appendix A), the statistical analysis (Appendix B), and some 90 letters attached to the returned questionnaires. We are not reporting the results of a scientific opinion poll. The Committee wishes to make it clear that this report represents the views of the six members of the Committee aided by the materials furnished to it. At this time, we wish to thank the many members of the Association and a considerable number of nonmembers for their assistance.

The Setting

The Committee wishes to point out that any consideration of the four matters referred to it is circumscribed by the times in which we live. Medicine itself is changing rapidly; so rapidly that it seems to be exploding in many directions. The pace of advance in the science and art of medicine constantly amazes all of us. A year seldom passes without a new medical organization or health agency being born. Performance over a period of years may be necessary to determine whether these new organizations or agencies are genuinely medical or largely devoted to fund raising. This rapid pace of change has many other manifestations in our field of endeavor. Indeed, historians may record that the greatest accomplishment of the 20th century was that men learned how to die old instead of young. Apparently this greatest period of rapid mortality decline has run its course as the expectation of life at birth is now creeping upward very slowly from 69 years to 70 years. A continuation of the earlier rapid rise in this important statistical measure of life awaits further important developments in the medical management of the diseases of older life.

You have directed us to reexamine four important aspects of our Association. Every professional organization needs an occasional reevaluation. Your request comes at a time when the success of medicine in terms of length of life has reached a high and, at present, a rather stable level. For these great gains in the length of life the American people are grateful to us and to our fellow scientists. In our analysis of our Association, we have steadfastly kept in mind that the unique function of our profession which has distinguished it from other professions is that we have life on our hands. We are also mindful that in recent years medicine may

have suffered more from its successes than from its failures. Progress in postponing death has come so rapidly in the past several decades that we must now recognize that the rate of progress can scarcely be continued at its frenzied pace. We make these brief observations in this preamble because these and other great factors are a part of the pattern provided us by our times; the problems of the American Medical Association are very much a part of the entire American scene. There are, of course, many socioeconomic factors involved even as there are in other fields about us. Among these are technology, industrialization, urbanization, unionization, inflation, and the rising percentage of older voters.

Asking for Criticism

When any long-established organization attempts rigorous self-criticism, some of its members and many outsiders may lift their eyebrows and question that it can be done. However, we submit that our attempts to obtain criticism have been highly successful. We have read and heard both favorable and unfavorable criticisms of every major activity of the Association and of every Headquarters' department; some were stated in rather vigorous language. The Committee is not confronted with an undersupply of criticisms. Moreover, the Committee is now convinced that a survey of the type such as we have conducted should be repeated every three or five years. In general, we would like to reassure the House that the volume of information we have received is quite sufficient for our purposes. Our problem is to utilize this wealth of material most effectively.

A few general comments on these preliminary observations seem warranted. Your Committee has been impressed with the great variety of ideas expressed. Interesting side lights have also been noted. For example, some of the extreme criticisms we received remind us of the young socialist who liked to banter his opposition with "I have a plan for increasing government control in the field of medicine. You don't have a plan for more government control. Therefore, I am doing positive thinking and your approach is negative and reactionary." Another side light was the unusual suggestion of a few respondents that the A. M. A. should immediately develop and insist on a minimum wage for interns and for residents. It will repay one to read all the 1,600 selected quotations in Appendix A. You will note many other side lights.

If it can be said that these many and varied criticisms point in any central direction, it would be that the central problem of our Association in the year 1958 is "splintering"—the dynamics of medicine are driving us in so many directions simultaneously. The result is more and ever more divisions and subdivisions in the practice of medicine. One may justly ask, is medicine organized or disorganized? The central imperative for our Association is to re-establish its leadership, and unify the fragments into a cohesive entity under one umbrella.

The Questionnaire Survey

Copies of this report, together with the appendixes, were mailed to the members of the House several weeks in advance of this meeting. We may now turn to a review of the questionnaire survey on each of the four topics assigned to us by the House. These topics were captioned A, B, C, and D in the questionnaire. Additionally, we include our findings and recommendations. At this point in our report we shall consider only the highlights of the statistical analysis of Appendix B.

During May our questionnaire was mailed to all members of the House and alternate delegates. It was also sent to the officers and trustees, 13 past-presidents, the editors of state and county society journals, the secretaries or executive secretaries of state and county medical societies, the secretaries of the American Boards, the national organizations of medical interest (listed periodically in THE JOURNAL), the deans of medical schools, and members of A. M. A. councils and committees. We shall refer to these as the black questionnaires because they were printed in black ink. Of this total of 2,938 mailed, 521, or 18%, were returned by the cutoff date for key punching and tabulation, July 11. (Actually 522, not 521, black questionnaires were used in the statistical analysis; see the first table in Appendix B for the number of usable returns and requested questionnaires.) The county medical societies accounted for 1,904 of the 2,938 black questionnaires mailed; 245 replies or 13% were returned; excluding the questionnaires sent to the county societies, the return was 27%. The members of the Committee were puzzled by the 34% return from the members of the House. However, we do recognize the pressures of time and circumstance, and are confident that the response obtained reflects a dependable consensus of that body.

The same questionnaire was printed in blue ink and mailed to 3,924 members and nonmembers, a probability sample, consisting of every 60th name in the punch card file. Only 497, or 13%, were returned; and 32 were unusable. Frankly, the Committee had expected a higher percentage of returns, considering the amount of publicity given to the project. The two most important explanations are that this type of request for criticism of the Association is new and the four topics assigned to the Committee and incorporated in the questionnaire are inherently difficult. The Committee was greatly pleased, however, by the wide scope of the replies as indicated by the selected quotations of Appendix A. Moreover, as set forth in detail in Appendix B, the 465 respondents to the blue questionnaire were a good cross section of the entire probability sample of 3,924 members and nonmembers as to age and state of residence. (The black questionnaires were sent to a stratified sam-

ple of persons holding certain positions.) Although the Committee was not trying to take a poll, the representativeness of the relatively small number of respondents to the blue questionnaire strongly suggests that a larger response would have added little to the Committee's knowledge. Over and above these technical considerations, your Committee recognizes that its task was to weigh and interpret the specific criticisms received and present to this House a series of observations and recommendations on each of the four topics assigned to it. Although our report will review the results as if there were four separate compartments corresponding to the four separate assignments given the Committee by the House, certain types of comments appear and reappear among the responses to all questions; for example, comments of a socioeconomic nature appear in the responses to every question although the Committee designed Part D for that purpose.

Part A

(Redefinition of the central concept of A. M. A. objectives and basic programs.)

The Committee instructed the staff of the Bureau of Medical Economic Research to break up each question, particularly those requesting comments, into a series of subquestions or categories to be phrased by the Bureau staff after an examination of several hundred replies. In editing the replies to Part A, it was found that 13 subquestions or categories could be used in coding and editing the replies to all three questions (see list of subquestions in Appendix A):

1. What is your idea of what the A. M. A. does for you? For the American public?
2. What do you think the objectives, aims, and goals of the A. M. A. should be?
3. Do you have suggestions for improving the service and effectiveness of the A. M. A.? Yes ☐ No ☐ If yes, please give them.

For example, many of the suggestions for improving the service and the effectiveness of the Association under question 3 were very similar to what other respondents suggested as the objectives, aims, and goals in question 2. Likewise, some of the respondents gave objectives, aims, and goals requested under question 2 in their replies to question 1 about what the A. M. A. does for you and for the American public. This same intermingling of questions 1, 2, and 3 was also noted in the 90 letters attached to the returned questionnaires. Thus, the responses to the three questions of Part A were considered under 13 subquestions or categories thereby displacing the original three questions. The essential unity of Part A has been preserved, but the separate quality of the three questions thereunder is somewhat blurred by this procedure. The five categories or subquestions mentioned most frequently by the respondents were numbered 2, 4, 5, 6, and 9.

2. *Scientific Information:* Improving, advancing. Dissemination to physician. Physician's informal post-grad. Publications, J. A. M. A., advertising. Scientific assemblies, exhibits. Research.
4. *Practice of Medicine:* Standards; maintaining or improving. Protection of M.D. Prestige. Osteopaths, relations with.
5. *Organization of Profession:* Leadership, official representation, coordination. Spokesman for profession, spokesman for physicians. Parent organization. Integration of groups within A. M. A. (e. g. Specialty and G. P.). Inter-group relationships within profession. Medical policies; positive vs. negative stand. Communication, county and state societies, and national level.
6. *Socioeconomic and Political Areas:* Study and dissemination of information. Representative spokesman for profession. Lobby. Physician's union. Socioeconomic and political policy. Cooperation with other professions and self-employed groups. Free choice of physician. Socioeconomic problems. Distribution of physicians. Cost of medical care. Insurance.
9. *Medical Care for Public:* Advancing, improving, individual and public health. Protection against quacks, improper drugs. Investigations.

The typical respondent to each of these questions mentioned two of these 13 categories or subquestions. In giving the replies to the three questions, 987 respondents "checked" a total of 5,726 of these 13 categories or subquestions. A total of 1,113 mentioned some objective or activity of a socioeconomic nature (number 6); 851 mentioned some phase of the organization of the profession (number 5). The differences in the rank order of the tabulations for the black and the blue questionnaires were not very marked. Among the black questionnaires the third most frequent response dealt with medical care for public (number 9), but practice of medicine (number 4) ranked third among the blue questionnaires. The subquestion or category ranked fourth among the black questionnaires was scientific information (number 2); among the blue questionnaires, medical care for public (number 9). Although the tabulations of these three questions set forth in Appendix B are worth study for the details provided, we conclude at this point that insofar as the responses received in our questionnaire survey are concerned, the socioeconomic function of our Association looms largest in the minds of our members. The 90 thoughtful letters and the reflections of the Committee further substantiate this conclusion.

As a result of these observations, your Committee concludes that the membership of the A. M. A. is convinced that the sociological and economic trends and conditions of today constitute an important aspect in the medical care of the patient and of the practice of medicine. Along with medical education, diagnostic medicine, therapeutic medicine, preventive medicine, Public Health medicine, and medical research—the art and science of medicine—sociological and economic aspects are integral parts of the unlimited health care of the people.

We, therefore, **recommend** that this House of Delegates consider the advisability of amending Article II of the Constitution by this substitution:

"The objectives of the Association are to promote the science and art of medicine and the betterment of public health, and an understanding of the socioeconomic conditions which will facilitate the attainment of these objectives."

Additional suggestions in the socioeconomic area are presented later in this report.

Part B

(Placing more emphasis on scientific activities.)

The second area, Part B, which the Committee was asked to investigate was scientific activities. Our broad interpretation of this was that we were to advise the House as to whether the scientific activities of the Association were generally adequate, generally inadequate, or about right. This was a large order for the questionnaire which we wanted to limit to 10 questions. (As has been pointed out already, some of our best information on one of the four parts of the questionnaire was actually included in the reply to another part.) The three questions follow:

4. Does the present degree of emphasis placed upon scientific activities by the American Medical Association meet with your approval? Yes ☐ No ☐ (Comments regarding specific activities will be appreciated by the Committee.)

5. Have you attended a midwinter Clinical Session? Yes ☐ No ☐ Do you consider these sessions valuable?

6. The Committee solicits your comments, if you have any, on the work of the A. M. A. bureaus, committees, councils, departments, divisions, and other agencies listed below. Please attach a reply if the lines provided below are not sufficient.

1. Bureau of Health Education
2. Bureau of Medical Economic Research
3. Committee on Legislation
4. Council on Constitution and Bylaws
5. Council on Industrial Health
6. Council on Medical Education and Hospitals
7. Council on Medical Service
8. Council on Mental Health
9. Council on National Defense
10. Council on Rural Health
11. Council on Scientific Assembly
12. Department of Public Relations
13. Division of Councils of Therapy and Research
    14. Council on Drugs
    15. Council on Foods and Nutrition
    16. Council on Medical Physics
    17. Bureau of Investigation
    18. Chemical Laboratory
19. General Manager's Office
20. Law Department
21. Judicial Council
22. Records and Circulation Department
23. Scientific Publications & Library
24. Today's Health
25. Washington Office

Of the returned black questionnaires, 86% indicated that the present degree of emphasis on scientific activities met with the approval of the respondents; the percentage on the blue questionnaires was 76. This overwhelmingly affirmative reply from those who chose to respond does conceal some of the important observations which the members of the Committee have read in the selected quotations in Appendix A. A few respondents claimed that many papers in THE JOURNAL were apparently chosen on the basis of when and where delivered rather than content and that the journals and the meetings of the specialty organizations were more valuable from the scientific standpoint.

In the matter of the Clinical Session, the number responding to the black questionnaire who had attended and who had not attended a clinical session was about equal, whereas the respondents to the blue who had not attended were about two and one-half times as numerous as those who reported they had attended. On the question of whether the midwinter Clinical Session is valuable, the ratio of "yes" to "no" on the black questionnaire was 5 to 1; and 4 to 1 on the blue questionnaire. In both groups, however, one-third to one-half did not reply.

The major purpose of question 6 was to set forth the 25 bureaus, committees, councils, divisions, and departments. Unfortunately, this question was left blank on more than half of the black and the blue questionnaires; fewer than one-third made specific comments on one or more of the 25 listed agencies of the Association. (See selected quotations in Appendix A.) A number of respondents wrote that this list of 25 agencies was an education to them; indeed, this was the primary purpose of the Committee in listing them. It was also felt that this list of 25 agencies might help respondents in answering other questions. Typically, respondents on the black questionnaire who gave a specific reply referred to three of these agencies and those on the blue questionnaire to two. It was very difficult to edit and code the responses to this question which might be said to have 25 parts. The first attempt was to classify the responses as favorable or unfavorable for the agency concerned. For example, consider a respondent who after indicating disagreement with a specific A. M. A. policy severely criticized the agency which published items in support of that policy. Should this reply be considered favorable or unfavorable criticism of the specified agency? Since no agreement could be reached on a consistent pattern of interpretation of comments as being favorable or unfavorable and the replies were so few, the Bureau of Medical Economic Research was asked merely to tabulate the number of mentions of each of the 25 agencies. Despite the small number of replies, it may be helpful to note that the Council on Medical Education and Hospitals, the Department of Public Relations, the Washington Office, and the Council on Drugs were mentioned (favorably or unfavorably) most frequently.

The conclusion of Part B on the subject of whether our Association should or should not place more emphasis on scientific activities is that there are no widespread dissatisfactions with the Association's present emphasis on scientific activities as a whole, so far as is revealed by a mere count of the replies of the respondents. But the selected quotations (see Appendix A) and our own obser-

vations indicate some measure of dissatisfaction. Scientific progress is never-ending. Your Committee strongly **advises** the Board of Trustees to give serious consideration to the establishment of some more effective mechanism to insure continued study of the scientific activities of the Association with the ultimate intent and purpose of revamping and otherwise changing them as deemed necessary. Your Committee understands that there is already a "special committee to study scientific activities," but it is believed that the scope of the "special committee" is too limited. This thought about the scope of a study of scientific activities of the Association will be more fully developed in a section of this report to follow.

Part C

(Taking the lead in creating more cohesion among national medical societies.)

The third part of the Committee's assignment was to examine the need for creating more cohesion among national medical societies. Questions 7 and 8 of Part C were designed to provide the Committee with specific advice on this problem of the relationship of our Association to other national medical organizations with an invitation for comments on question 7, but not on question 8.

7. Do you approve of the present relationship between the American Medical Association and other national medical organizations? Yes ☐ No ☐ (The Committee would welcome your suggestions for changes in the relationship of the A. M. A. to a named national medical organization[s].)

8. Do you believe that independent action among national medical societies promotes or impedes progress toward the goals of the medical profession? Promotes ☐ Impedes ☐

If you believe that more cohesion among national medical societies is desirable, please indicate in which of the three areas: Scientific ☐ Socioeconomic ☐ Both ☐

Among the respondents to the black questionnaire a ratio of better than 3 to 1 approved the present relationships; check marks on the blue questionnaire agreed with the ratio of more than 3 to 1. This was a very general appraisal of our relationships with the other national organizations. Although the comments offered in addition to the check marks were fewer than we had hoped, it is apparent that some respondents doubt that the A. M. A. is still the recognized leader of the profession. This type of comment was also given in Parts A and B. Others believe that more coordination is desirable particularly in regard to the meetings of the other national organizations—a comment which might have been given to question 8 if the Committee had provided lines for comments. There was a wide scatter of other comments, but the relationships with the American College of Surgeons and the American Academy of General Practice were featured. The phrases excerpted from the comments on question 7 provided the Committee with some illuminating details.

The Committee sought to obtain additional light on this problem of relationships by asking only for check marks in question 8. The replies on the black questionnaire produced a tie on the question of whether independent action among national medical societies promotes or impedes progress toward the goals of the medical profession. Recognizing that we are reporting to you information derived from a small sample, we believe that this even division between the pros and cons is worth noting. Among the respondents to the blue questionnaire, the ratio was about 3 to 2, three "promotes" and two "impedes." In our desire to offer you a few objective questions requiring only check marks for your answers we did not invite comments regarding what "promotes" and what "impedes" progress toward our goals in the first part of question 8. The Committee was aided, however, by comments on the question of relationships with other national medical societies which were recorded among the responses to other questions.

From the replies to this second part of question 8 it is clear that the respondents believe that more cohesion is needed in both scientific and socioeconomic areas, with somewhat more stress on the latter. Moreover, the respondents to the black and the blue questionnaires were generally in agreement, although the latter placed slightly more stress on the scientific areas than did the former. In other words, the respondents, whether they thought independent action promotes or impedes progress toward the goals of the medical profession, told us that more cohesion among national medical societies is desirable. In the light of what the Committee learned from the responses to Part C, from the phrases excerpted from the replies to the other parts of the questionnaire, and on the basis of our own observations and discussions with a wide variety of physicians, we recommend that a more thorough study should be made of our relationships with other national medical organizations with a view to improving them and to reasserting A. M. A. leadership in socioeconomic areas particularly and to the maximum extent in scientific areas.

In order to accomplish these objectives, we **recommend** that the Board of Trustees in establishing a mechanism for the continued study of the scientific activities of the A. M. A. insure that that mechanism will assume the responsibility for establishing active liaison with each national medical society. The intent of this liaison should be to explore all fields of interrelationship between the A. M. A. and the national medical societies. There should be an attempt to define the area of activity of each organization. In the scientific fields the role of the A. M. A. might be primarily that of coordination between the special fields of scientific interest of the other national medical organizations. Improved cohesion between these organizations and the A. M. A. could result if the A. M. A. were to abolish its scientific sections and invite these national organizations to furnish the specialty and General Practice programs at each annual session. This possibility at least deserves study, and if it

were to prove practicable, the participating other national medical organizations might be given the representation in the House of Delegates vacated by the scientific sections as they are abolished.

In view of the many comments in Appendix A concerning the voluntary health agencies, it is equally important to insure that the mechanism for continued study of scientific activities of the Association include provision for the establishment of close liaison with those health agencies for the mutual benefit of the agency, the profession, and the public.

Part D

(Studying socioeconomic problems.)

The fourth part of our assignment was to study socioeconomic problems. As already noted, comments of a socioeconomic nature were prominent in the responses to Parts A, B, and C of the questionnaire. So great was the ground swell of comments of this character that we could not compartmentalize them in Part D. Question 9 was our second objective type question requiring a Yes or No answer, on a choice of three socioeconomic policies.

9. How far should the A. M. A. go in the socioeconomic field? Please check one of the following three: a. Should the A. M. A. limit itself to matters of prime concern to the health of the people of the nation? Yes ☐ No ☐. b. **Or** should the A. M. A. interest itself in socioeconomic factors of America which affect the health of the people of our nation and the practice of medicine? Yes ☐ No ☐. c. **Or** should the A. M. A. also interest itself in socioeconomic issues whether or not they directly affect the health of the people of our nation or the practice of medicine? Yes ☐ No ☐ .

10. What socioeconomic policies of the A. M. A. do you approve or disapprove?.....

A number of respondents answered more than one of the three, but the overwhelming proportion of check marks on policy "b" provided us with a definitive answer.

Socioeconomic policy "a" was not popular. In the black questionnaires the single responses were 35 to "a," 281 to "b," and 93 to "c"; considering respondents who checked more than one answer, those stressing policy "a" numbered 57, "b" numbered 364, and "c" numbered 154. The responses on the blue questionnaires present substantially the same result with great emphasis on policy "b."

Your Committee concludes, therefore, that the A. M. A. should not "limit itself to matters of prime concern to the health of the people of the nation." It should "interest itself in socioeconomic factors which affect the health of the people of our nation and the practice of medicine." Supported by the results of the returned questionnaires and other sources, we would conclude that the A. M. A. should not interest itself in "socioeconomic issues whether or not they directly affect the health of the people of our nation or the practice of medicine." We submit that a comprehensive history of the American Medical Association would indicate that policy "a" was favored in an earlier era. Indeed, we believe that policy "c," the almost unbounded scope of socioeconomic interest, may well be the policy toward which our Association is now moving. Obviously, a constantly increasing number of our members realize that good health is dependent not only upon good medical care but also upon good food, good clothing, good housing and good sanitation as well, and that their dual responsibility as physician and citizen makes imperative an active participation by their Association in any and all legitimate activities directed toward that goal. We commend these findings to this and future sessions of the House of Delegates without specific recommendations for changes in the Constitution or the establishment of a 10-point or 20-point socioeconomic program.

The tremendous emphasis in this questionnaire survey on socioeconomic policies was one of the surprises to our Committee. It seems that no matter which questions we asked about objectives and policies, and/or how we worded them, the socioeconomic aspects were somehow emphasized by respondents. (See Appendix B.) No longer can it be claimed that our Association is not interested and should not be interested in socioeconomic factors of American life.

In framing question 10 the Committee thought it wise not to specify socioeconomic policies by name. Responses indicating general approval, though few in number, greatly exceeded responses indicating general disapproval of Association policies. Almost half of the respondents commented on one or more specific policies. In coding and editing the responses, 19 policies were mentioned often enough to warrant tabulation. As stated in the preamble, we consider it of critical importance that the House positively know this to be a committee's report and not a statistical report of the results of a scientific poll of opinion. Hence, it would serve no purpose to report on the tabulations separately for and against a specific policy. Approval or disapproval of the Association's stand on socialized medicine was mentioned most frequently, with approval or disapproval of the Association's position on social security coverage for self-employed physicians ranking second, followed by approval or disapproval of Association policy on the extension of voluntary health insurance. The fourth most popular item was approval or disapproval of what we were forced to call "publicizing policies." As noted, many of the responses to other questions have provided useful information to the Committee on socioeconomic policies. Curiously, the Forand bill and the third party problem ranked below all four of these policies.

Part E

(Classification of Respondent.)

The last section of this questionnaire survey, Part E, provided for the classification of the respondent. As shown in Appendix B, the distributions by age and by state of those who responded

to the blue questionnaire and those who did not respond were quite similar. Although the IBM punch card file could not be used for testing the representativeness of the respondents as to type of practice, form of active private practice, and size of city, the fact that the distributions by age and by state were reasonably similar suggests that the respondents were representative of the entire group of 3,924 in the probability sample to whom blue questionnaires were mailed. This fact fortifies the Committee's confidence in the questionnaire survey results. Since the black questionnaires were sent to a stratified sample in which the number of county medical society secretaries loomed so large, a similar test of the representativeness of the respondents to the black questionnaires was not even attempted.

Most of the respondents on the black questionnaire reported that they are A. M. A. members, as did more than four-fifths of those who responded to the blue questionnaire in the probability sample. We are pleased to report that 9 out of 10 respondents to the black questionnaire signed it; and 8 out of 10 who responded to the blue questionnaire did likewise.

General Conclusions

In the foregoing we have set forth our findings, suggestions, and some recommendations on each of the first three topics which you assigned to our Committee. We turn now to more general conclusions including our recommendations on the fourth topic.

First, the members of the Committee were in unanimous **agreement** that it should be **discharged** although the task is not finished. Indeed, our studies definitely indicate this to be a continuous task. A reasonably complete set of recommendations would require more study and consideration of the setting provided by the rapidly changing medical, economic, social, and political events of our times, such as a continuous study would eventually reveal. Periodic self-examination is highly desirable, especially at this juncture in the development of our Association, the practice of medicine, and the rapidly changing social scene in the United States.

Second, we **recommend** the establishment for a period of three years of a Council or Committee on Socioeconomics to investigate socioeconomic and related problems with which the Association is likely to be confronted in future years. This council or committee could be of five members who should be appointed by our President, the Speaker of our House, and the Chairman of our Board of Trustees. This council or committee should have power to hold conferences with any and all individuals or groups who might develop ideas of aid to our Association and its purposes. This council or committee should report to the Board of Trustees and to the House of Delegates. During its three-year tenure, this committee or council should find its place in our Association activities and the House and Board of Trustees should review its work thoroughly before its activities are continued beyond the three-year period. Your Committee hopes that the materials we have provided will chart a course for this new council or committee.

Third, your Committee **recommends** that the Board of Trustees give serious consideration to opening the publications of the Association to a free and open discussion of socioeconomic problems applicable to medicine. Members and officers of the Association should be encouraged to contribute items to this section of the publication, or publications; and a special invitation should be extended to the many able persons on our Headquarters' staff. In the words of a member of our Committee, "We must restore to our members the feeling of belonging." We must not stifle constructive criticism; forward-looking discussions of any and all future problems should be made available to our members.

The Committee is thoroughly convinced that the A. M. A. must vigorously reassert its leadership in American medicine. We must cease the splintering tactics so disastrous to French politics. We must not become a disorganized profession. A more vigorous and more deliberately developed socioeconomic program toward this end is imperative.

At this point, your Committee wishes to direct special attention to the time-consuming, painstaking, thoroughgoing, and most effective work performed by Dr. Frank G. Dickinson and his staff, Dr. Leonard W. Martin, research associate, Olga Stetsuk and Cynthia Harkness, research assistants, of the Bureau of Medical Economic Research.

From the outset of our activities, Dr. Dickinson gave us expert counsel and guidance in the preparation of the questionnaire and in the method of its distribution among our members and nonmembers. In innumerable other ways he brought to our activities the experience and perspective of the expert statistician which are invaluable to any survey; but particularly so in the sensitive area of socioeconomic policies applicable to the American Medical Association.

We would especially emphasize the manner in which Dr. Dickinson and his staff have analyzed the responses to the questionnaire, have broken them down into subquestions, and have catalogued these responses in a manner designed to make our task much easier and our report more meaningful. The selection of some 1,600 quotations from the returned questionnaires—an ingenious procedure—presented in Appendix A has made us feel that the respondents were invisible members of our Committee. The statistical analysis of the returned questionnaires (Appendix B) reflects the consensus of an important cross section of informed and interested physicians throughout the country.

Finally, we wish to thank again all members and nonmembers who have counseled with us, those who returned their questionnaires, and particularly those who wrote us the 90 letters of more than 180 pages.

James Z. Appel
Thurman B. Givan
Hugh H. Hussey Jr.
Raymond M. McKeown
Milford O. Rouse
Lewis A. Alesen, *Chairman*

REPORT OF REFERENCE COMMITTEE

Report of Committee to Study A. M. A. Objectives and Basic Programs.—Your reference committee has spent an unusual amount of time in studying the report of the Committee to Study A. M. A. Objectives and Basic Programs and in listening to the free discussion in the open session. Truly heartening is the tremendous interest manifested by the respondents to the questionnaires, by oral discussions in small groups, and by the spirited review before the reference committee. It may be that this report will be a most significant milepost in the history of the American Medical Association.

With the far-reaching changes that have evolved in the socioeconomic and political areas of this country, it is logical that an organization such as the A. M. A. can profitably take stock of its expressed objectives or purposes, and its basic programs of service and activity. The work of this Committee has proved that American physicians can evaluate themselves professionally, and as citizens; can recognize areas of needed improvement; and can outline practical ways of maintaining the highest standards of health in this country, within the framework of private enterprise, the truly American way of life.

In a sincere desire to stimulate progress in medicine in every specialty and area, the A. M. A. has encouraged specialty societies, and it is only natural that in the multiplicity of medical groups the stature and prestige of the parent organization may not be so apparent. But it is easily possible for the A. M. A. to continue as the "fountainhead" of virile, worthwhile scientific groups, and yet sponsor such a bold, vigorous, constructive, logical program that its leadership will be recognized and respected more than ever before.

Clearly the members of the A. M. A. are convinced that sociological and economic trends and conditions of today constitute an important aspect in the medical care of the patient and of the practice of medicine.

Your reference committee recommends that the first recommendation of this special committee—that the House of Delegates consider amendment of Article II of the Constitution by this substitution: "The objectives of the Association are to promote the science and art of medicine and the betterment of public health and an understanding of the socioeconomic conditions which will facilitate the attainment of these objectives"—be referred to the Council on Constitution and Bylaws.

Your reference committee recommends that the Board of Trustees establish a mechanism which will assume the responsibility for promoting active liaison with each national medical society. The intent of this liaison should be to explore all fields of interrelationship between the A. M. A. and the national medical societies. There should be an attempt to define the area of activity of each organization. In the scientific fields the role of the A. M. A. might be primarily that of leadership, but every endeavor should be made to bring about coordination of the special fields of scientific interest of the other national medical organizations.

Since the Board of Trustees in Supplementary Report L has announced a very comprehensive plan to establish and develop a Division of Socio-Economic Activities, your reference committee feels that there is no necessity for the creation of a new council or committee on socioeconomics. The House of Delegates will be informed periodically on the progress of this new Division of Socio-Economic Activities through the medium of semi-annual reports to the House and the regular media of publications.

Your reference committee approves the recommendation that the Board of Trustees give serious consideration to opening the publications of the Association to a free and open discussion of socio-economic problems applicable to medicine. Members and officers of the Association should be encouraged to contribute items to this section of the publication or publications.

The Committee to Study A. M. A. Objectives and Basic Programs has served faithfully and correctly points out that the assignment given to it by this House last December was so comprehensive that no one group could be expected to cover the responsibilities completely, particularly in the space of a few months.

Since it is apparent to your reference committee that the work of analysis and improvement of basic programs of the A. M. A. will continue through the mechanisms mentioned in this report, this special committee should be relieved of further responsibility and we so recommend, with the additional recommendation of an expression by this House of Delegates of deep appreciation and thanks for a task well done. Special thanks are also due Dr. Frank G. Dickinson and his staff of the Bureau of Medical Economic Research for the tremendous service rendered in preparing this report. We urge every delegate to study his copy of the report very carefully and urge every physician to review with interest the printed summary and other comments in THE JOURNAL.

G. B. WILDER, M.D., Indiana
C. F. STROSNIDER, M.D., North Carolina
P. P. THOMPSON, M.D., Maine
W. F. COSTELLO, M.D., New Jersey
J. B. COPELAND, M.D., *Chairman*, Texas

MEDICAL NEWS

COLORADO

Dr. von Kaulla Participates in Broadcast.—Dr. Kurt N. von Kaulla, a member of the University of Colorado School of Medicine faculty, recently participated in a discussion which was recorded for broadcast throughout Europe by the Voice of America. He is one of four German-speaking researchers invited by the U. S. State Department to take part in the recorded discussion during a symposium on blood conducted at Wayne State University, Detroit. The 15-minute transcribed discussion concerned, among other subjects, progress made in America in dissolving blood clots. On the panel with Dr. von Kaulla were three research scientists visiting in the U. S., and representing Germany, Austria, and the Netherlands.

ILLINOIS

Meeting of Anesthesiologists.—The Illinois Society of Anesthesiologists will convene March 21 at the Lincoln Room, Edgewater Beach Hotel, Chicago, with dinner at 7 p. m. and the scientific program beginning at 8 p. m. "The Limitations of Anesthesia in Poor Risk Patients" will be given by Dr. James E. Eckenhoff, professor of anesthesiology, University of Pennsylvania, Philadelphia. Reservations for dinner ($5.30) must be made not later than March 14. For information and reservation write Dr. Frank M. Grem, 546 N. Elmwood Ave., Oak Park, Ill.

Engineers Aid Medical Research.—Thirty-five Illinois Bell Telephone Company engineers have volunteered their know-how to help medical research in fighting cancer, heart disease, and infant deaths. New instruments resulting from their spare-time efforts were demonstrated Feb. 5 for the first time at the University of Chicago. The volunteers belong to an organization called SAVE—Service Activities of Volunteer Engineers. They have reported that accomplishments of the first year of work included:

1. Completion of working models of a three-ounce device to count the human heartbeat while being worn during a full day of normal activity.
2. Virtual completion of a training machine to teach laboratory technicians to identify cancer cells under the microscope.
3. Progress toward an electronic computer that instantaneously reports changes in the volume of air in the lungs of a baby in the hope of detecting hyaline membrane disease.
4. Progress toward an electronic circuit 10 times more sensitive than existing equipment to radiation from radioisotopes trapped in brain tumors.
5. Under development is an electronic calorimeter, which is a cumulative recording device to measure changes in body heat. Such an instrument would aid in studies of metabolism.

Another device is an electronic stethoscope. The idea for SAVE originated with William V. Kahler, president of Illinois Bell and a trustee of the University of Chicago. After consulting with physicians at the University of Chicago Clinics, the engineers set to work in basements, garages, and workshops at their homes in 20 suburbs and throughout Chicago. All the instruments developed through the efforts of SAVE reportedly will be put at the disposal of the medical profession. An enlarged report on SAVE will appear in the Medicine at Work section of THE JOURNAL, issue of March 21.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

Chicago

Dr. Cooper Honored.—Dr. John A. D. Cooper, professor of biochemistry and assistant dean of Northwestern University Medical School, recently was honored by the University of Brazil when it conferred on him the degree of Doutor Honoris Causa, "in recognition of the work done in helping to establish and equip a radioisotope laboratory in the Institute of Biophysics at the university's medical school."

Annual Medical History Lecture.—The annual D. J. Davis Memorial Lecture on Medical History will be given at 1 p. m., Wednesday, April 22, in Room 221 of the Dental–Medical–Pharmacy Building of the University of Illinois, 1853 W. Polk St. The lecturer will be Dr. Lloyd G. Stevenson, professor of the history of medicine and dean of the Faculty of Medicine, McGill University, Montreal P. Q., Canada. His subject will be "The Early Development of Internal Medicine in the United States."

Lectures in Research in Cancer.—The last two lectures in the University of Chicago 1959 Winter Quarter series on Research in Cancer are arranged as follows: March 9, 5 p. m., "The Contribution of Experimental Gliomas to Human Disease," Dr. Harry M. Zimmerman, chief, Laboratory Division, Montefiore Hospital, New York City; March 16, 5 p. m., "Viral Etiology of Mouse Leukemia: Its Possible Implications for the Problem of Cancer," Dr. Ludwik Gross, chief, Cancer Research Unit, VA Hospital, Bronx, N. Y.

Hospital News.—Michael Reese Hospital and Medical Center has announced the appointment of Dr. Morris Weiss to the position of first Medical Director of Mandel Clinic, the Hospital's out-patient division. In this new position, Dr. Weiss, who was assistant professor of medicine, Baylor University College of Medicine, Waco, Texas, from 1956 to 1957, will be responsible for all medical care and education given at the clinic.

KANSAS

Centennial for State Society.—On Feb. 10 the charter issued by the Territorial Legislature of Kansas was 100 years of age and the Kansas Medical Society which was given "perpetual succession forever" survived its first century. The centennial is to be commemorated until the close of the annual session to be held in Topeka, May 4-6. A special program based on a frontier theme necessitates that the meeting be held at the Fairgrounds. Many events for public participation have been planned. A Hall of Health with educational exhibits for the public will be open for two weeks prior to the annual session. A book, "A Century of Medicine in Kansas," has been written with the cooperation of the Committee on History. The National Rural Health Conference at Wichita March 5-7, is also a part of the society's centennial celebration.

MAINE

Conference on Mental Retardation.—The first International Medical Conference on Mental Retardation, organized by the Maine Chapter of the American Academy of Pediatrics, the Division of Maternal and Child Health, Maine Department of Health and Welfare, and the Pineland Hospital and Training School, Pownal, will be held July 27-31 at the Eastland Hotel, Portland. The program will include in its five days of general sessions addresses on brain anatomy, the reticular system, head anomalies, phenylketonuria, lipoids, birth injury, embryology, infections, mongolism, erythroblastosis, therapy, psychiatry, psychology, and behavior disorders, by "outstanding authorities" on these subjects. Not intended to answer all questions on the problems concerning mental retardation but rather to construct the problems which have to be attacked scientifically, the conference is open to all physicians throughout the United States, Canada, and other countries, following immediately after the International Pediatric Congress at Montreal, Canada. For information write Dr. Ella Langer, State of Maine, Department of Health and Welfare, Augusta, Maine, Chairman, Arrangements Committee.

MARYLAND

Hygiene Lecture.—As part of the De Lamar Lectures in Hygiene of the School of Hygiene and Public Health, The Johns Hopkins University, Baltimore, a public lecture on "The Long Range Effects of Ionizing Radiations on the Individual" was presented by Dr. William R. S. Doll, lecturer in medical statistics and epidemiology, London School of Hygiene and Tropical Medicine, England, Feb. 20.

MASSACHUSETTS

Medical History Meeting.—The next meeting of the Benjamin Waterhouse Medical History Society will be a combined meeting with the Providence Medical Historical Society to be held at the Massachusetts Memorial Hospital, Monday, March 16. Dr. Seebert J. Goldowsky, director, Peripheral Vascular Clinic, Rhode Island Hospital, will be the speaker, presenting, "The Hospital at Portsmouth Grove." For information and reservations write Dr. John J. Byrne, 818 Harrison Ave., Boston 18, Secretary (KE 6-8600).

Dr. Bandler Named Department Chairman.—Dr. Bernard Bandler, of Cambridge, president-elect of the American Psychoanalytic Association, has been named chairman of the department of psychiatry at the Boston University School of Medicine. He has also been named psychiatrist-in-chief of the Massachusetts Memorial Hospitals. He has been associated with the school and with the hospital since 1947. Dr. Bandler is currently chairman of the Ad Hoc Committee on Education in Public Hospitals of the American Psychiatric Association in liaison with the American Psychoanalytic Association, a member of the executive committee of the American Psychoanalytic Association, training analyst for the Boston Psychoanalytic Society and Institute, Inc., and a member of the Medical Advisory Committee of Boston University's Sargent College.

MICHIGAN

Sight Testing for Children.—The eyesight of 325,837 Michigan school children was screened in 1958 by technicians employed by local health departments and local schools, the Michigan Department of Health has reported. Each child was screened for nearsightedness, farsightedness, astigmatism, and muscle imbalance. Of the children screened, 37,035 (11.5%) were referred to doctors to have an eye examination for the first time. During 1958, 57 children were added to the state health department's Register of Children with Severe Visual Handicaps. Nine hundred and thirty-nine youngsters are now registered, 187 whom are of preschool age.

MISSOURI

Dr. Sante Receives Radiology Award.—Dr. LeRoy Sante, professor of radiology and director of the department, Saint Louis University School of

Medicine, received a gold medal award from the American College of Radiology at ceremonies in Chicago Feb. 6, during the college's annual convocation. Dr. Sante was one of three radiologists throughout the country unanimously chosen for the award by the board of chancellors of the college. The gold medal award is presented annually "for distinguished and extraordinary service to the American College of Radiology and to the profession for which it stands." The award also will be presented posthumously to Dr. C. Edgar Virden, formerly chief of the radiologic service at St. Joseph's Hospital, Kansas City, Mo., and to Dr. Robert S. Stone, director of the department of radiology, University of California.

MONTANA

Joint Meeting in Missoula.—The Montana Heart Association and the Montana Trudeau Society will sponsor a joint meeting in Missoula, April 17-18. All sessions will convene at the Florence Hotel and all physicians and interested lay people are invited. The speakers at this meeting will include Dr. Herbert E. Griswold, chairman, department of cardiology, University of Oregon Medical School, Portland; Dr. Richard E. Fowler, professor of pediatrics, Tulane University School of Medicine, New Orleans; Dr. Walter M. Kirkendall, clinical associate professor of internal medicine, State University of Iowa College of Medicine, Iowa City; Dr. David T. Smith, professor of bacteriology and associate professor of medicine, Duke University School of Medicine, Durham, N. C.; Dr. Jay A. Myers, professor of internal medicine, University of Minnesota Medical School, Minneapolis; and Dr. Carroll J. Martin, Seattle Sanitarium.

NEW JERSEY

Dr. Stevenson Named Department Chairman.—Dr. Stuart S. Stevenson was appointed professor and chairman of the department of pediatrics, Seton Hall College of Medicine, Jersey City. Dr. Stevenson, whose appointment was effective March 1, comes to Seton Hall from the University of Pittsburgh School of Medicine, where he has been acting chairman of the department of pediatrics. In addition, he was acting medical director and chief of staff at the Children's Hospital in Pittsburgh. He is chairman of the Committee on Residency Fellowships of the American Academy of Pediatrics.

NEW YORK

Dr. Weinberg to Lecture on Hypnosis.—The New York County Chapter of the American Academy of General Practice will present Dr. Abraham Weinberg, chairman, Committee on Mental Hygiene, New York Academy of General Practice, and lecturer in medical hypnosis, Seton Hall College of Medicine, March 12, 9 p. m., room 65 at the Academy of Medicine, 2 E. 103rd St., New York City. Dr. Weinberg will discuss "Indications and Techniques of Hypnosis for the General Practitioner." For information write Dr. Stanley H. Greenwald, 325 E. 79th St., New York 21, Secretary.

Personal.—The provisional appointment of Dr. Ray K. Brown as associate director of the State Health Department's Division of Laboratories and Research effective Jan. 29, has been announced by Dr. Herman E. Hilleboe, state health commissioner. Dr. Brown has served since 1953 as assistant director of the department's Laboratories for Biochemistry and Immunology.—Dr. James W. Bartlett Jr. has been named assistant dean of the University of Rochester School of Medicine and Dentistry. He is in charge of admissions and will assist in administration of scholarships and loans. Dr. Bartlett is an instructor in the department of psychiatry.

OHIO

Dr. Dods to Give Rachford Lectures.—The 27th annual series of the Benjamin Knox Rachford lectureships will take place in Cincinnati April 21 and 22, at 8:30 p. m. Dr. Lorimer F. Dods, professor of child health at the University of Sydney, Australia, will deliver these lectures in the auditorium of the Children's Hospital Clinic and Research Building. On April 21 Dr. Dods will lecture on "Pædiatrics in the Antipodes," and on April 22 his subject will be "Some Pædiatric Philosophy."

PENNSYLVANIA

Bicentennial Week in Pittsburgh.—The Pittsburgh Bicentennial Lecture Week in Medicine was held during the last week in February. Four lectures were presented in the University of Pittsburgh Schools of the Health Professions auditorium. Guest lecturers were Theodore T. Puck, Ph.D., chairman, department of biophysics, University of Colorado School of Medicine, Denver; Dr. George W. Thorn, Hersey professor of theory and practice of physic, Harvard Medical School, Boston; Dr. Carl V. Moore, chairman, department of medicine, Washington University School of Medicine, St. Louis; Dr. Charles W. Mayo, head, surgery section, Mayo Clinic, Rochester, Minn.

Philadelphia

Annual Lecture.—The Kappa Pi Chapter of the Phi Delta Epsilon Fraternity will hold its annual Bernard Comroe lectureship series March 20 in the Medical Alumni Hall of the Hospital of the University of Pennsylvania. The guest speaker will be Dr. Harold G. Wolff, professor of medicine (neurology), Cornell University Medical College, New York City. His subject will be "Headache."

Dr. Koprowski Receives French Award.—Dr. Hilary Koprowski, director of the Wistar Institute of Anatomy and Biology and president of The New York Academy of Sciences, received the cross of a commander of the Ordre du Merite pour la Recherche et l'Invention from the Societe d'Encouragement pour la Recherche et l'Invention (French) at a ceremony in the Wistar Institute museum Feb. 11. The Societe d'Encouragement pour la Recherche et l'Invention was formed in 1901 under the sponsorship of the French government ministries of education, public health, and industry and commerce. A committee composed of authorities in the various fields of science chooses a few researchers and inventors of high standing each year for awards of various degrees in the society's Ordre du Merite. Dr. Koprowski is chairman of the Inter-American Society of Microbiologists and a member of the virology and rickettsiology study section of the National Institutes of Health.

TEXAS

Steel Company Donates Community Hospital.—Hospital in the Pines, a 30-bed hospital costing more than 30 million dollars and built by the Lone Star Steel Company, was turned over to the people at a formal dedication ceremony recently. The president of the company, Mr. E. B. Germany, presented the title to the board of directors. The gift of the hospital was noncommittal, and the Steel Company will have no voice in the hospital management. The board of seven members will be entirely independent of the company. Mr. Thomas K. Ewan, chairman of the board, accepted the hospital in behalf of the board at the ceremony. In the spring of 1956 Lone Star Steel employed an independent firm of hospital consultants to determine the site that would best serve the area. Local civic and business leaders organized Hospital in the Pines, Inc. and the charter was granted in 1957. The design will permit later expansion. Dr. Lowell E. Rutledge, of Daingerfield, is chief of staff.

GENERAL

Fellowships in Forensic Pathology.—Under the auspices of the College of American Pathologists, there is a vacancy for a fellow in forensic pathology for a period of six months' training at the Armed Forces Institute of Pathology. Stipend is $2,500. Six months' credit toward the Subspecialty Certificate in Forensic Pathology given by the American Board of Pathology will be allowed to the individual filling this fellowship. Interested individuals may apply to the AFIP or to Dr. Russell S. Fisher, Chairman, Committee on Forensic Pathology, College of American Pathologists, Prudential Plaza, Chicago.

Fraternity Meeting in Miami Beach.—The seventh annual interim scientific meeting of Phi Lambda Kappa, national medical fraternity, will be held at the Deauville Hotel, Miami Beach, Fla., April 5-12. The five-day program, starting Monday, April 6, will be for the benefit of the general practitioner and will feature papers and symposiums by specialists in their fields. All members of the medical and dental professions are welcome. For registration and information, write Dr. Samuel L. Lemel, 1621 Euclid Ave., Cleveland 14.

Tri-State Association Meets in Winston–Salem.—The annual meeting of the Tri-State Medical Association for Virginia, North Carolina, and South Carolina will be held March 16-17 in Winston–Salem, N. C. Five panel discussions are arranged: "Gastroenterology," "Dermatology," "Psychiatry," "Cardiac," and "Trauma." The following papers will be presented:

Urology—A New Surgical Approach for the Correction of Urinary Incontinence, Dr. L. T. Pennington, Greensboro, N. C.
Infertility, Dr. John Monroe, Winston–Salem, N. C.
Hypnosis in Pregnancy, Dr. T. W. Littlejohn, Durham, N. C.
Radiation Hazards, Dr. I. Meschan, Winston–Salem, N. C.

Guest speaker at the banquet at 7 p. m., March 16, will be Dr. Robert F. Clodfelter, of Winston–Salem.

Meeting on Anesthesia Research in Miami Beach.—The 33rd congress of the International Anesthesia Research Society will be held April 20-23 in Miami Beach, Fla. Papers to be presented by foreign participants include the following:

Anesthesia for the Ambulant Surgical Patient, Dr. Eric Webb, Vancouver, British Columbia, Canada.
A Method of Anaesthesia for Per-Oral Endoscopy, Dr. J. D. A. Firth, Montreal, Quebec, Canada.
Anesthetic Techniques for Tonsillectomy and Adenoidectomy in Children, Dr. Oscar V. Ribeiro, Rio de Janeiro, Brazil.

Three panel discussions are planned: "Open Cardiac Surgery," "Recurrent Staphylococcal Infections in Modern Hospitals," and "Pharmacology." Two movies are scheduled, and discussions will conclude each session.

Aero Medical Meeting in Los Angeles.—The 30th annual meeting of the Aero Medical Association will be held April 27-29 at the Statler Hilton Hotel, Los Angeles. Brig. Gen. M. S. White, M. C., USAF, president of the association, will open the program with an address, followed by the Louis H. Bauer Lecture, presented by Dr. Hans Selye, Faculty of Medicine, University of Montreal, on "Stress in Aviation Medicine." Two symposiums are planned: "Aeromedical Aspects of Stress," with Dr. Selye as chairman, and "Toxicological Health Hazards," with Col. Harold V. Ellingson, M. C., USAF, director of education and plans, USAF School of Avia-

tion Medicine, Randolph Air Force Base, Texas, as chairman. The program will include speakers from Canada, England, Italy, France, Germany, and Norway. For information write Dr. T. H. Sutherland, P. O. Box 26, Marion, Ohio, Secretary.

Southwestern Meeting on Nuclear Medicine.—The fourth annual meeting of the Southwestern Society of Nuclear Medicine will be held in the Roosevelt Hotel, New Orleans, March 14-15, under the presidency of Dr. Herbert C. Allen Jr., Houston, Texas. The program includes 17 scheduled papers and three panel discussions with the following titles and moderators:

Some Aspects of Isotope Use in Studies of Electrolyte Metabolism, Dr. Sam A. Threefoot, New Orleans, La.
Medical Management in Radiation Accident Cases, John Hidalgo, M.S., New Orleans, La.
Symposium on Scintillation Scanning, Dr. Herbert C. Allen Jr., Houston, Texas.

The business meeting and dinner are planned for the evening of March 14. For information write Dr. Samuel B. Nadler, 1520 Louisiana Ave., New Orleans 15, chairman of the program committee.

Proctology Meeting in New York City.—The 11th annual convention of the International Academy of Proctology will be held at The Plaza, New York City, April 5-9. The international, national, and local program committees are planning a seminar on practical techniques for office and hospital. There will be special emphasis on anal and rectal panel presentations, and on newer treatment methods, as requested by those who attended the Mexico City meeting in 1958. Motion-picture demonstrations are planned. Members and nonmembers of the academy and their wives are invited to the banquet April 8. The Women's Auxiliary has planned a program for the wives and their guests. There is no fee for attendance at these teaching sessions of the academy. For information, write the International Academy of Proctology, 147-41 Sanford Ave., Flushing, N. Y., Dr. Alfred J. Cantor, Executive Secretary.

Allergists Meeting in San Francisco.—The 15th congress of the American College of Allergy will be held March 15-20 at the Mark Hopkins Hotel, San Francisco. A graduate instructional course in allergy will be conducted March 15-17. Dr. Merle W. Moore, president of the college, will speak at the general session March 18. On March 19 a panel discussion, "Repository Injection Treatment of Inhalant Allergy," will be moderated by Dr. Lawrence J. Halpin. Dr. Max Samter, president, American Academy of Allergy, will present "Semantics —and the Future of Allergy" the afternoon of March 19. Sectional sessions will be conducted March 20 under the following headings: Dermatologic Allergy, Psychosomatic Medicine, Technology, and Pediatric Allergy. Tours, movie sessions, and exhibits are planned. For information write the American College of Allergy, 2049 Broadway, Boulder, Colo.

Triological Society Meeting in Hot Springs, Virginia.—The American Laryngological, Rhinological, and Otological Society, Inc., "The Triological Society," will meet March 10-12 at the Homestead, Hot Springs, Va. A business meeting will precede each session. The presidential address will be given by Dr. Gordon D. Hoople, Syracuse, New York. Speakers on the program are as follows: Drs. George F. Reed, Boston; John J. O'Keefe, Philadelphia; Robert E. Boswell, Dayton, Ohio; John F. Daly and Samuel Rosen, New York City; Walter E. Heck, Robert C. McNaught, Leonard G. Dobson, and Francis S. Greenspan, San Francisco, Calif.; Victor R. Alfaro, Washington, D. C.; George E. Shambaugh Jr. and Henry B. Perlman, Chicago; Lester A. Brown, Atlanta, Ga.; Miles L. Lewis Jr., New Orleans; Bruce Proctor, Detroit; Maurice Schiff, Oakland, Calif.; Clair M. Kos, Iowa City; and Howard P. House, Los Angeles. For information write C. Stewart Nash, 708 Medical Arts Building, Rochester 7, New York, Secretary.

Nigerian Physician Wins Rehabilitation Award.—The appointment of Dr. Badejo O. Adebonojo of Nigeria as the recipient of the "Betsey Barton Fellowship" in Rehabilitation of the World Rehabilitation Fund has been announced by the fund's president, Dr. Howard A. Rusk. The "Betsey Barton Fellow" in rehabilitation, to provide advanced training in rehabilitation in the United States for a physician from Africa or Asia, was made possible by a grant to the World Rehabilitation Fund from the Aaron E. Norman Fund, Inc. The fellowship was named in honor of Miss Betsey Barton "because of her leadership in extending and expanding rehabilitation services throughout the world." Miss Barton, who is a paraplegic, is a member of the Board of Directors of the National Paraplegia Foundation, Inc., and of the board of Trustees of the Institute for the Crippled and Disabled. Dr. Adebonojo will begin his advanced training March 1 at the Institute of Physical Medicine and Rehabilitation, New York University–Bellevue Medical Center, New York City. The World Rehabilitation Fund, Inc., is a nonprofit organization supported by American industry, foundations, and individuals to assist in the international development of rehabilitation services for the physically handicapped.

Annual Southern Conference on Gerontology.—"Society and the Health of Older People" will be the theme of the ninth annual Southern Conference on Gerontology, to be held on the campus of the University of Florida, Gainesville, March 19-20. The program will deal primarily with "psycho-

social aspects of wellness and illness." Sessions will be devoted to the challenge of optimum health in old age; anthropological, sociological, and psychological aspects of health; social factors in the health of the elderly as seen from the standpoint of the physician, the social worker, the nurse, and the biologist; and public and professional aspects of the health care of the aged. Participants include Dr. Halbert L. Dunn, chief, National Office of Vital Statistics; Marion T. Loftin, Ph.D., of Mississippi State College; Ethel Shanas, Ph.D., of the University of Chicago; Robert W. Kleemeier, Ph.D., of Washington University (St. Louis); Carter C. Osterbind, Ph.D., of the University of Florida; Dr. Samuel Gertman, of the University of Miami; and Dr. Albert V. Hardy, of the Florida State Board of Health. For information write Irving L. Webber, Ph.D., Institute of Gerontology, Peabody Hall, University of Florida, Gainesville, or Robert L. Fairing, Ph.D., General Extension Division, Gainesville. The meetings are sponsored by the Institute and the General Extension Division of Florida.

Youth Fitness Week.—A Presidential Proclamation designating May 3-9, 1959, as National Youth Fitness Week, reads as follows:

WHEREAS the ongoing strength of our Nation depends upon health of our young people; and

WHEREAS we must always strive to improve the fitness of our youth by determined and coordinated efforts; and

WHEREAS, in this challenging world, it is essential that our young people recognize their obligation to themselves, to their families, and to the Nation, to endeavor to keep themselves mentally, emotionally, spiritually, socially, and physically fit; and

WHEREAS the President's Council on Youth Fitness has recommended that a National Youth Fitness Week be designated:

NOW, THEREFORE, I, DWIGHT D. EISENHOWER, President of the United States of America, do hereby proclaim the week beginning May 3, 1959, as National Youth Fitness Week.

I request officials of the Government, and I urge parents, young people, and interested local and national organizations, to use all appropriate means during that week to promote programs and activities demonstrating the importance of youth fitness to the end that we may assure the continuing strength and wellbeing of our people.

In Witness Whereof, I have hereunto set my hand and caused the Seal of the United States of America to be affixed.

Done at the City of Washington this thirty-first day of January in the year of our Lord nineteen hundred and fifty-nine and of the Independence of the United States of America the one hundred and eighty-third.

Dwight D. Eisenhower

Report on Age and Mortality.—Despite the marked progress made in reducing mortality in the United States, 40% of all deaths still occur at ages under 65, according to statisticians of the Metropolitan Life Insurance Company. More than 670,000 deaths a year are at ages under 65. Included were about 108,000 babies less than a year old and more than 400,000 people in the 45-64 year age bracket. Most deaths among infants are associated with pathological conditions existing prior to birth or with the hazards of the birth process, the statisticians point out. Three-fifths of the mortality results from "diseases of early infancy," a category comprising mainly deaths attributed to premature birth, postnatal asphyxia, and injuries at birth. Congenital malformation accounts for an additional 14% of infant deaths. In the mortality for the 1-24 age group, accidents are responsible for a greater number of deaths than all other causes combined, even among the girls. Among boys at these ages, motor vehicle accidents alone account for more than one-quarter of the deaths. In the 25-44 age group, the diseases of the heart, arteries, and kidneys account for nearly a third of the deaths among the males, with accidents a close second. Among women at these ages, cancer heads the list of causes of death. At ages 55-64 diseases of the heart, arteries, and kidneys account for nearly three-fifths of the deaths among men and for more than half the total among women. Second in rank is cancer, which accounts for 20% of the deaths among men and nearly 30% among women.

Education Foundation Has Record Campaign.—The 1958 campaign for the American Medical Education Foundation resulted in a record total of $1,120,044 plus interest, according to John W. Hedback, executive secretary of the Foundation. State and county AMEF committees raised the amount from physicians during the year. The grants to 85 medical schools were made at the 55th annual Congress on Medical Education and Licensure in Chicago, Feb. 7-16. The 1958 fund represents a 15% increase over 1957 totals. Thirty-five states reported increases, ranging from $9.06 (Nebraska) to $31,000 (New Jersey). The total dollar increase amounted to $148,000. Indiana, after one year as a dues-increase state, reported $30,600, for a total two and a half times that of a year ago. Alaska jumped from $125 in 1957 to $1,414.50 in 1958—an increase of 1,131%. Other spectacular climbs were made by Idaho (342%) and South Carolina (281%). Illinois physicians contributed $200,191, placing them first in the nation. California followed with $171,611. Both are dues-increase states. Arizona's 1958 total of $12,600 includes $1,000 from retail druggists. The amount stems from a program initiated late in the year through which druggists send gifts to AMEF in physicians' names in lieu of Christmas gifts. The plan was endorsed by the Arizona Retail Druggists Association. The Woman's Auxiliary to A. M. A. established a new record themselves with contributions of $126,200. Delaware, Maryland, Massachusetts, New York, Ohio, Texas, and Washington, D. C., all reported sizeable increases over 1957—ranging from $2,350 to $14,300 for an average of $6,000.

Contest for Paper on Gastroenterology Research.—The American College of Gastroenterology has announced the establishment of an award contest for the best unpublished paper on research in gastroenterology or an allied field. This award is to be known as the Henry G. Rudner Sr. Award, honoring Dr. Henry G. Rudner Sr., of Memphis, Tenn., chairman of the Research Committee of the American College of Gastroenterology and former chairman of the board of governors of the organization. This contest will be open to all those possessing the degree of doctor of medicine from a recognized medical school or university. All papers submitted must represent original work in gastroenterology, or an allied field, and must not have been previously published except for abstracts or short preliminary reports. It must not have been previously presented on the program of any scientific meeting. The papers may be on clinical or basic science; clinical papers must not be case records, but controlled clinical work. The length of a paper is no criterion for originality or value. All entries for the 1959 award must be typewritten in English, double-spaced on one side of the paper, and submitted in six copies. The award will be made at the annual convention banquet of the college, in Los Angeles, in September, 1959. The prize will be an award of $750 plus an additional $250 for traveling expenses. The paper selected for an award becomes the property of the American College of Gastroenterology and the decision of the judges will be final. All entries must be received no later than June 1 and should be addressed to: The Research Committee, American College of Gastroenterology, 33 W. 60th St., New York 23.

Committee on Bioastronautics.—The National Academy of Sciences–National Research Council announced the organization of the Armed Forces–National Research Council Committee on Bio-Astronautics. The committee will advise the Armed Forces, on their request, in any matter concerning the biological or medical aspects of space exploration. Policy decisions and the programming of activities within the committee will be the responsibility of an executive council to which the following scientists have been appointed by Dr. Detlev W. Bronk, president of the Academy–Research Council: chairman, Otto H. Schmitt, Ph.D., department of physics, University of Minnesota; vice-chairman, Melvin Calvin, Ph.D., department of chemistry, University of California, Berkeley; Howard J. Curtis, Ph.D., department of biology, Brookhaven National Laboratory; Paul M. Fitts, Ph.D., department of psychology, University of Michigan; Brig. Gen. Donald D. Flickinger, directorate of life sciences, Air Research and Development Command; Dr. John D. French, department of anatomy, University of California Medical Center, Los Angeles; Capt. Charles F. Gell, Office of Naval Research; James D. Hardy, Ph.D., U. S. Naval Air Development Center, Johnsville, Pa.; and Col. Robert H. Holmes, Research and Development Command, Office of the Surgeon General, Department of the Army. The full Committee on Bio-Astronautics—which will consist of more than 100 members, of whom at least half will be nominees of the Armed Forces—will serve as a conference or forum of active investigators, meeting periodically to review scientific and technical problems, exchange information, and establish liaison between investigators with allied interests. Administrative responsibility for the committee has been vested within the Academy–Research Council's Division of Medical Sciences, whose chairman is R. Keith Cannan, ScD. Acting executive secretary to the committee is Dr. Sam F. Seeley.

Directory of Blood Facilities.—A directory and description of blood facilities and services has been released by the Joint Blood Council, a nonprofit national organization with headquarters in Washington, D. C. It shows the location of facilities, the extent of their operations, how they are organized, what specific services they offer, and other information of importance to physicians, hospitals, and any person or organization interested in blood and its derivatives. The directory is based on data obtained from a questionnaire sent to all known blood banks, hospitals, and clinics that offer blood-handling services. The questionnaire was sent to 3,150 institutions and 2,202 replied. Those that failed to return the information will have an opportunity to supply it for future directories. The directory will be distributed free by the council to all institutions and organizations that participated in its preparation, according to Dr. Frank E. Wilson, executive vice-president. Others may obtain it at the cost price of $1.50 each from the Joint Blood Council headquarters, 1832 M Street, N. W., Washington 6, D. C. The council was formed three years ago by the American Association of Blood Banks, the American Hospital Association, the American Medical Association, the American National Red Cross, and the American Society of Clinical Pathologists "to establish a national blood program in order to assure an adequate supply of blood and blood derivatives to the civilian and military population at all times of peace or emergency and to take all appropriate action in connection therewith." Information includes the following: (1) Of the facilities listed, 1,832 administer whole blood. Also, 1,287 administer plasma, 1,021 serum albumin, 994 packed red blood cells, and 311 platelets, with many of the facilities engaging in a number of these activities. (2) Artery banks are maintained by 116, eye banks by 36, bone banks by 200, skin banks by 24, and mother's milk banks by 20. (3) A total of 1,325 blood banks store whole blood, record donor histories, and have as their primary purpose the

recruitment of donors and complete laboratory blood processing. (4) Two out of every three organizations listed have no reciprocity system for the exchange or resupply of blood. Of the remaining one-third, 470 use the American Red Cross system, 240 that of the American Association of Blood Banks, and 110 use both systems. Dr. Leonard W. Larson is president of the Joint Blood Council.

FOREIGN

International Course on Tomography.—The fourth International Course on Tomography will be held at the Radiology Institute, University of Genoa, Italy, under the direction of Prof. Alessandro Vallebona. This course will last eight days and deal particularly with the recent progresses in tomographical methods. The period September-October, 1959 has been chosen for this meeting. All lectures, while read in the original language, shall be contemporarily translated into Italian, French, English, German, and Spanish. All interested physicians are advised to write Prof. Neopolo Macarini, General Secretary, Instituto di Radiologia della Universita–Ospedale San Martino, Genova, Italia, for information.

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners: Part II only, April 21-22; Parts I and II, June 16-17; Part I only, Sept. 9-10. Examinations must be received at least six weeks in advance of a specific examination date. Examining centers established after close of registration. Exec. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia 4.

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates, Inc.: Stations around the world, Feb. 17. Deadline for foreign applications was Nov. 17. The following examination will be held Sept. 22 with application deadline of June 22. Exec. Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Ill.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Written.* Montgomery, June 16-18. Sec., Dr. D. G. Gill, State Office Bldg., Montgomery 4.

ALASKA:* On application in Anchorage and Juneau. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

ARKANSAS:* *Examination and Reciprocity.* Little Rock, June 11-12. Sec., Dr. Joe Verser, Harrisburg.

CONNECTICUT:* *Regular. Examination.* Hartford, March 10-12. Acting Sec., Dr. Stanley B. Weld, 160 St. Ronan St., New Haven.

FLORIDA:* *Examination.* Miami Beach, June 22-24. Sec., Dr. Homer L. Pearson, 901 N.W. 17th St., Miami 36.

GEORGIA: *Examination and Reciprocity.* Atlanta, June. Sec., Mr. C. L. Clifton, 224 State Capitol, Atlanta 3.

GUAM: *Subject to Call.* Act. Sec., Dr. F. L. Conklin, Agana.

MICHIGAN:* *Examination.* Ann Arbor and Detroit, June 8-10. Sec., Dr. E. C. Swanson, 118 Stevens T. Mason Bldg., West Michigan Ave., Lansing 8.

MINNESOTA:* *Reciprocity.* St. Paul, February. Sec., Dr. F. H. Magney, 230 Lowry Medical Arts Bldg., St. Paul.

MONTANA: *Examination and Reciprocity.* Helena, April 7. Sec., Dr. Thomas L. Hawkins, 535 Fuller Ave., Helena.

NEBRASKA:* *Examination.* Omaha, June 15-17. Director, Mr. Husted K. Watson, Room 1009, State Capitol Bldg., Lincoln 9.

NEW JERSEY: *Examination.* Trenton, June 16-19. Sec., Dr. Royal A. Schaaf, 28 West State St., Trenton 8.

NEW MEXICO:* *Examination and Reciprocity.* Sante Fe, May 18-19. Sec., Dr. R. C. Derbyshire, 227 East Palace Ave., Santa Fe.

NORTH CAROLINA: *Examination.* June Asst. Sec., Mrs. Louise J. McNeill, 716 Professional Bldg., Raleigh.

OKLAHOMA:* *Examination.* Oklahoma City, June 2-3. Exec. Sec., Mrs. E. L. Haidek, 813 Braniff Bldg., Oklahoma City.

OREGON:* *Written.* Portland, Apr. 17-19. Ex. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland 4.

SOUTH CAROLINA: *Reciprocity.* Columbia, May 12; *Examination.* Columbia, June 23-24. Sec., Dr. H. E. Jervey, Jr., 1829 Blanding St., Columbia.

TEXAS:* *Examination and Reciprocity.* Fort Worth, June 22-24. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

UTAH: *Examination.* Salt Lake City, July 8-10. Dir., Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City 1.

VIRGINIA: *Examination.* Richmond, June 18-20. *Endorsement.* Richmond, June 17. Address: Board of Medical Examiners, 631 First St., S. W., Roanoke.

WISCONSIN:* *Written.* Milwaukee, July 14-16. *Reciprocity.* Madison, April 17 and Milwaukee, July 15. Sec., Dr. Thomas W. Tormey, Jr., 1140 State Office Bldg., Madison.

WYOMING: *Examination and Reciprocity.* Cheyenne, June 1. Sec., Dr. Franklin D. Yoder, State Office Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARKANSAS: *Examination.* Little Rock, May 4-5. Sec., Dr. S. C. Dellinger, University of Arkansas, Fayetteville.

DISTRICT OF COLUMBIA: *Examination.* Washington, May 18-19. Address: Mr. Paul Foley, Deputy Director, 1740 Massachusetts Ave., N. W., Washington.

FLORIDA: *Examination.* Miami, June 6. Sec., Mr. M. W. Emmel, University of Florida, Box 340, Gainesville.

IOWA: *Examination.* Des Moines, April 14. Sec., Dr. Elmer W. Hertel, Wartburg College, Waverly.

KANSAS: *Examination.* Kansas City, June. Sec., Dr. L. C. Heckert, Pittsburg.

MICHIGAN: *Examination.* Ann Arbor and Detroit, May 8-9. Sec., Mrs. Anne Baker, West Michigan Ave., 116 Stevens T. Mason Bldg., Lansing.

NEBRASKA: *Examination.* Omaha, May 5-6. Director, Mr. R. K. Kirkman, Bureau of Examining Boards, 1009 State Capitol Bldg., Lincoln.

OKLAHOMA: *Examination.* Oklahoma City, Mar. 27-28. Exec. Sec., Mrs. L. Haidek, 813 Braniff Bldg., Oklahoma City.

OREGON: *Written.* Mar. 7. Sec., Dr. Earl M. Pallett, Box 5175, Eugene.

TENNESSEE: *Examination.* Memphis, Mar. 25-26. Sec., Dr. O. W. Hyman, 62 South Dunlap St., Memphis 3.

TEXAS: *Examination.* Austin, Galveston, Houston, Apr. 17-18. Certificates issued by reciprocity and waiver on the first and fifteenth of each month. Sec., Bro. Raphael Wilson, 407 Perry-Brooks Bldg., Austin.

WISCONSIN: *Examination.* Madison, April 4. Final date for filing application is March 27. Milwaukee, June 6. Final date for final application is May 29. Sec., Mr. W. H. Barber, 621 Ransom St., Ripon.

*Basic Science Certificate required.

DEATHS

Bietsch, Charles Frederick, Pittsburgh; University of Pittsburgh School of Medicine, 1913; specialist certified by the American Board of Obstetrics and Gynecology; an associate member of the American Medical Association; fellow of the American College of Surgeons; associated with the Mercy Hospital and the Roselia Foundling and Maternity Hospital; died Dec. 6, aged 71.

Brownell, William Flockton Ⓜ Fort Collins, Colo.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1898; specialist certified by the American Board of Otolaryngology; fellow of the American College of Surgeons; past-president of the Larimer County Medical Society; veteran of World War I; on the staff of the Larimer County Hospital; died Dec. 5, aged 84.

Burpee, Benjamin Prescott, Manchester, N. H.; Harvard Medical School, Boston, 1914; veteran of World War I; president of the New Hampshire Board of Registration in Medicine; associated with the Elliot Hospital, where he died Nov. 27, aged 69.

Bushard, Bruce Lauren Ⓜ Lieut. Colonel, U. S. Army, Washington, D. C.; Northwestern University Medical School, Chicago, 1947; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association; service member of the American Medical Association; veteran of World War II; entered the regular Army in 1948; died Dec. 10, aged 36.

Chisholm, Julian Ford Sr. Ⓜ Savannah, Ga.; University of Maryland School of Medicine, Baltimore, 1900; fellow of the American College of Surgeons; past-president of the Georgia Ophthalmological Club; member of the Seaboard Air Line Railway Surgeons Association; veteran of World War I; for more than 40 years oculist for the Seaboard and Central of Georgia Railways; on the staffs of the Telfair Hospital, Central of Georgia Railway Hospital, and St. Joseph's Hospital; died Dec. 13, aged 82.

Clark, Daniel Ennis, Parkersburg, W. Va.; University of Louisville (Ky.) School of Medicine, 1945; formerly a captain in the medical corps, Army of the United States; died Dec. 21, aged 42.

Clarke, Thomas Greene, Hyannis, Mass.; Tufts College Medical School, Boston, 1911; veteran of World War I; died in the Cape Cod Hospital Dec. 17, aged 70.

Ⓜ Indicates Member of the American Medical Association.

Cohen, Herman Ⓜ New York City; Columbia University College of Physicians and Surgeons, New York City, 1905; died in the Morrisania Hospital Nov. 26, aged 77.

Cruikshank, Alexander Ⓜ Detroit; McGill University Faculty of Medicine, Montreal, Que., Canada, 1895; died Dec. 15, aged 87.

Cunningham, Robert Blythe Ⓜ Booneville, Miss.; Tulane University School of Medicine, New Orleans, 1926; fellow of the American College of Surgeons; veteran of World War I; vice-president of the Prentiss County Home Bank; member and past-president and secretary of the staff of the Northeast Mississippi Hospital, where he died Dec. 13, aged 61.

Cunningham, William Harry Ⓜ Rockford, Ill.; Chicago College of Medicine and Surgery, 1909; veteran of World War I; served on the staff of St. Anthony Hospital; died in Pittsburgh Dec. 1, aged 77.

Davidson, Alfred Ⓜ Chelsea, Mass.; Tufts College Medical School, Boston, 1910; also a graduate in pharmacy; on the staff of the Chelsea Memorial Hospital; died Dec. 14, aged 78.

Delzell, David Deronda Ⓜ Toledo, Ohio; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1912; on the staff of the Riverside Hospital; died Dec. 22, aged 73.

Dillard, James Bascom Ⓜ Davisboro, Ga.; Atlanta Medical College, 1894; also a graduate in pharmacy; served as president of the Washington County Medical Society; died Nov. 18, aged 86.

Dillon, John Alfred Jr. Ⓜ Austin, Texas; University of Kansas School of Medicine, Kansas City, 1935; service member of the American Medical Association; veteran of World War II; a lieutenant colonel and flight surgeon in the U. S. Air Force Reserve; died in the USAF Hospital at Lackland Air Force Base Nov. 18, aged 49.

Durrill, Everett Lee Ⓜ Pueblo, Colo.; Northwestern University Medical School, Chicago, 1931; fellow of the American Psychiatric Association; specialist certified by the American Board of Psychiatry and Neurology; on the staff of the Colorado State Hospital; died in Georgetown Dec. 3, aged 54.

Eakins, Olin Martin, Miami Beach, Fla.; Columbia University College of Physicians and Surgeons, New York City, 1899; an associate member of the

American Medical Association; member of the Medical Society of the State of Pennsylvania; formerly medical director of the Reliance Life Insurance Company in Pittsburgh; died Dec. 23, aged 84.

Frank, Louis James Ⓜ Huntington, N. Y.; Long Island College Hospital, Brooklyn, 1910; served on the faculty of his alma mater; physician in charge of the venereal disease clinic for the New York Health Department; on the staffs of the Long Island College Hospital, Brooklyn Women's Hospital, and Kings County Hospital, all in Brooklyn; specialist certified by the American Board of Dermatology and Syphilology; member of the Brooklyn Dermatological Society; died Oct. 12, aged 70.

Friedman, David Dudley, Brooklyn; Long Island College Hospital, Brooklyn, 1924; died Nov. 7, aged 59.

Frizell, William Henry Ⓜ Brookhaven, Miss.; University of Nashville (Tenn.) Medical Department, 1897; past-president of the Mississippi State Medical Association and served as president of its Fifty Year Club; past-president of the Tri-County–Pike–Lincoln–Copiah–Walthall Counties Medical Society, of which he was secretary for many years; a director of the Mississippi division of the American Cancer Society; for many years county health officer; member of the state board of health from 1930 to 1936; a director of the Mississippi Hospital Medical Service (Blue Cross–Blue Shield); died in the King's Daughters Hospital Dec. 3, aged 86.

Furgason, Allen P., Lincoln, Neb.; Northwestern Medical College, St. Joseph, Mo., 1889; an associate member of the American Medical Association; died in Phoenix, Ariz., Nov. 13, aged 91.

Giering, Herman J., Baltimore; Baltimore University School of Medicine, 1898; died in the Church Home and Hospital Nov. 25, aged 83.

Golden, William Colyn Ⓜ Clanton, Ala.; Louisiana State University School of Medicine, New Orleans, 1935; staff member and board member at the Chilton County Hospital; died in Birmingham (Ala.) Hospital Dec. 17, aged 51.

Hammond, Robert Lee Ⓜ Jackson, Ga.; University of Georgia Medical Department, Augusta, 1920; medical director of the Butts County Health Department; died Dec. 8, aged 64.

Hanson, William Clinton Ⓜ Augusta, Maine; Harvard Medical School, Boston, 1905; member of the Massachusetts Medical Society; veteran of World War I; formerly practiced in Belmont, Mass., where for 32 years he was school physician; served as assistant and acting secretary of the Massachusetts Department of Health; awarded a gold medal by the international jury of awards at the Panama-Pacific Exposition in Washington in 1915; died in Farmingdale Dec. 10, aged 83.

Hargis, Frank Cooper, Nashville, Tenn.; Vanderbilt University School of Medicine, Nashville, 1901; died in Columbia Nov. 4, aged 81.

Healy, Joseph Cornelius, Lockport, N. Y.; St. Louis University School of Medicine, 1924; health officer of Pendleton and Lockport; on the staffs of the Millard Fillmore Hospital in Buffalo and the Lockport Memorial Hospital; died Dec. 15, aged 59.

Henry, Martin Rudolph Ⓜ St. Peter, Minn.; University of Nebraska College of Medicine, Omaha, 1925; since 1941 on the staff of the St. Peter State Hospital; died suddenly Dec. 10, aged 58.

Herrington, Van Dolph Ⓜ Pryor, Okla.; University of Oklahoma School of Medicine, Oklahoma City, 1925; on the staff of the Grand Valley Hospital; member of the New Mexico Medical Society; died Dec. 2, aged 63.

Herron, Henry Harrison Ⓜ Jackson, Tenn.; University of Tennessee College of Medicine, Memphis, 1934; veteran of World War II; associated with the Webb–Williamson Hospital and the Jackson–Madison County General Hospital, where he died Dec. 6, aged 46.

Herron, Thomas Basil Ⓜ Monessen, Pa.; University of Pittsburgh School of Medicine, 1911; veteran of World War I; medical director of the Pittsburgh Steel Company; served as school director and president of the board; president of Peoples National Bank & Trust Company until its merger with Mellon Bank and Trust Company, when he became a director; associated with the Charleroi–Monessen Hospital in Charleroi, where he died Dec. 3, aged 69.

Hibbert, Russell William Jr. Ⓜ Greeley, Colo.; born in Hannibal, Mo., Jan. 30, 1916; St. Louis University School of Medicine, 1939; served on the faculty of the University of Colorado School of Medicine in Denver; member of the American Rheumatism Association; veteran of World War II; in 1958 president of the Weld County Cancer Society; once served as a physician for the Greeley High School football team; in January, 1949, the Greeley Junior Chamber of Commerce presented him with its annual award of outstanding young man of the year; honored for his contributions to the community and its youth; in 1953 received the Silver Beaver Award for his contribution to Boy Scouting; died Dec. 4, aged 42.

Hift, Robert Ⓜ Chicago; Medizinische Fakultät der Universität, Vienna, Austria, 1909; clinical associate in medicine at the Chicago Medical School; associated with American, McKenna, Weiss Memorial, Mount Sinai, and Forkash Memorial hospitals; died Dec. 22, aged 74.

Hodge, Benjamin Ervin, Wilmington, Del.; Johns Hopkins University School of Medicine, Baltimore, 1924; specialist certified by the American Board of Pediatrics; physician in charge in the general services department of the Du Pont Company; formerly on the staff of Johns Hopkins Hospital, Baltimore, where he died Nov. 28, aged 59.

Hoerr, Normand Louis, Cleveland; Graduate School of Medicine of the Division of the Biological Sciences, University of Chicago, 1931; on the faculty of the Western Reserve University School of Medicine; formerly on the faculty of his alma mater; died Dec. 14, aged 56.

Hole, Melvin Leo Ⓜ Danville, Ill.; Northwestern University Medical School, Chicago, 1911; fellow of the International College of Surgeons and the American College of Surgeons; member of the Industrial Medical Association; past-president of the Vermilion County Medical Society; veteran of World War I; on the staffs of Lake View and St. Elizabeth hospitals; died in Phoenix, Ariz., Dec. 12, aged 70.

Hollander, Beatrice Elsie Sterling Ⓜ Philadelphia; Woman's Medical College of Pennsylvania, Philadelphia, 1941; died Dec. 11, aged 41.

Hooper, Lester E. Ⓜ Indianola, Iowa; Keokuk (Ia.) Medical College, College of Physicians and Surgeons, 1908; veteran of World War I; in 1958 received the Simpson College Award for community service; died Dec. 6, aged 71.

Huckaby, William Ramsey Jr., Huntsville, Ala.; University of Tennessee College of Medicine, Memphis, 1956; interned at the Confederate Memorial Medical Center in Shreveport, La., and served a residency at the City of Memphis Hospitals in Memphis; died Dec. 9, aged 28.

Huggins, Benjamin Harrison Ⓜ Santa Barbara, Calif.; the Hahnemann Medical College and Hospital, Chicago, 1916; specialist certified by the American Board of Internal Medicine; veteran of World War I; for many years on the consulting staff of the Illinois Masonic Hospital and on the attending medical staff, Cook County Hospital in Chicago; served on the staff of St. Francis Hospital in Evanston, Ill.; associated with St. Francis Hospital and the Santa Barbara Cottage Hospital, where he died Dec. 20, aged 70.

Hughes, Archibald William, Greenville, R. I.; Tufts College Medical School, Boston, 1906; died Dec. 10, aged 76.

Hulick, Charles Henry Ⓜ Shelbyville, Ill.; Eclectic Medical College, Cincinnati, 1911; associated with the Shelby County Memorial Hospital; served as president of the Chamber of Commerce; died Dec. 10, aged 70.

Huntley, Howard B. Ⓜ Kindred, N. D.; Northwestern University Medical School, Chicago, 1908; veteran of the Spanish–American War; associated with the St. Luke's Hospital and St. John's Hospital in Fargo, where he died Dec. 2, aged 82.

Jacquet, Edward Frederick, Morgan City, La.; Meharry Medical College, Nashville, Tenn., 1932; on the staff of the Lakewood Hospital, where he died Nov. 13, aged 53.

Jewell, Ernest Lemon Ⓜ Logansville, Wis.; Rush Medical College, Chicago, 1924; past-president of the Sauk County Medical Society; associated with the Reedsburg (Wis.) Municipal Hospital and the Richland Hospital in Richland Center; died Nov. 22, aged 62, of coronary thrombosis.

Jones, Jay Glen Ⓜ Chicago; Northwestern University Medical School, Chicago, 1911; member of the American Academy of General Practice; past-president of the North Shore Branch of the Chicago Medical Society; on the staff of the Grant Hospital, where he died Dec. 13, aged 73.

Kelly, Frank Leo Ⓜ Lieut. Commander, U. S. Navy, retired, Aberdeen, S. D.; St. Louis University School of Medicine, 1916; service member of the American Medical Association; entered the U. S. Navy in 1917 and retired Jan. 1, 1937; member of the American Society of Clinical Pathologists; died in St. Luke's Hospital Sept. 26, aged 67.

Kennedy, Charles Allen Ⓜ Taylorsville, Miss.; Memphis (Tenn.) Hospital Medical College, 1911; member of the American Academy of General Practice; died Dec. 16, aged 72.

Knowles, Donald Brewster Ⓜ Chicago; Northwestern University Medical School, Chicago, 1931; veteran of World War II; member of the Industrial Medical Association; past-president and vice-president of the Chicago Society of Industrial Medicine and Surgery; president of the medical staff of Roseland Community Hospital; on the staff of Jackson Park Hospital; head of the medical staff of the Acme Steel Company in Riverdale; died Dec. 29, aged 51.

Little, Robert Nathan Ⓜ Summerville, Ga.; University of Georgia Medical Department, Augusta, 1929; served as president of the Chattooga County Medical Society; died Dec. 1, aged 55.

Loewenstein, Gustav Joseph Ⓜ Rochester, N. Y.; Albertus–Universität Medizinische Fakultät, Königsberg, Prussia, Germany, 1923; served in the German Army during World War I; associated with Genesee and Park Avenue hospitals; died Dec. 9, aged 61.

Loveland, Horace Hall Ⓜ Escanaba, Mich.; Detroit College of Medicine, 1894; served as health officer of Tecumseh; died Dec. 15, aged 92.

Macdonald, James Herbert, Kennebunk, Maine; University of Toronto Faculty of Medicine, Toronto, Ontario, Canada, 1917; served in World War I as a captain in the medical corps with the Canadian Expeditionary Forces; awarded the Veteran of Foreign Wars "good citizenship medal"; York County medical examiner; a director of the Ocean National Bank and the Kennebunk Building and Loan Association; died in the Maine Medical Center, Portland, Dec. 2, aged 66.

MacKethan, David Gillespie, Fayetteville, N. C.; University College of Medicine, Richmond, 1899; also a druggist; died Dec. 7, aged 80.

McConnell, Thomas William Ⓜ Pittsburgh; Jefferson Medical College of Philadelphia, 1920; served on the staff of the Passavant Hospital; died in St. Clair Memorial Hospital Nov. 18, aged 64.

McIlhatten, Samuel Patterson, Doylestown, Pa.; Medico-Chirurgical College of Philadelphia, 1901; an associate member of the American Medical Association; served on the consulting staff of the Abington (Pa.) Memorial Hospital Dec. 7, aged 79.

McIlwain, Sam Terrell, Waynesboro, Miss.; Mississippi Medical College, Meridian, 1910; served for many years as surgeon for the Gulf, Mobile and Ohio Railroad; died Dec. 26, aged 74.

McNeer, Lewis C. Ⓜ Bristol, Tenn.; Maryland Medical College, Baltimore, 1904; College of Physicians and Surgeons, Baltimore, 1906; on the staff of the Bristol Memorial Hospital; died Dec. 10, aged 80.

Mahan, James Merton Clay Ⓜ Pittsburgh; University of Pittsburgh School of Medicine, 1913; died Dec. 5, aged 68.

Mansbacher, Kurt Ⓜ St. Louis; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1919; member of the Endocrine Society; served on the faculty of Washington University School of Medicine; a member of the staff of the Jewish Hospital; died Dec. 19, aged 63.

Marshall, Robert Bruce Ⓜ Sulphur, La.; Tulane University of Louisiana School of Medicine, New Orleans, 1927; member of the American Academy of General Practice; on the staff of the West Calcasliеu-Cameron Hospital; an honorary member of the board of directors of St. Patrick's Hospital in Lake Charles; died Dec. 9, aged 57.

Martin, Sylvia Parsons Blake, Hackensack, N. J.; Woman's Medical College of Pennsylvania, Philadelphia, 1897; died in the Holy Name Hospital, Teaneck Nov. 18, aged 85.

Mazique, Zealy Marion, Pine Bluff, Ark.; Meharry Medical College, Nashville, Tenn., 1904; died in the Davis Hospital Dec. 3, aged 83.

Megahan, Calvin Roy, Follansbee, W. Va.; Western Pennsylvania Medical College, Pittsburgh, 1907; member of the West Virginia State Medical Association; past-president and secretary of the Brooke County Medical Society; county health officer and coroner since 1942; died in the Ohio Valley Hospital, Steubenville, Ohio, Dec. 6, aged 74.

Menlowe, Patterson Morris Ⓜ McKeesport, Pa.; University of Pittsburgh School of Medicine, 1923; specialist certified by the American Board of Pathology; member of the College of American Pathologists and the American Society of Clinical Pathologists; associated with the McKeesport Hospital, where he served as medical director and director of laboratory, and where he died Dec. 18, aged 59.

Messmer, Clemens C. Ⓜ Milwaukee; Milwaukee Medical College, 1903; formerly on the faculty of the Marquette University School of Medicine; served on the staffs of St. Joseph's Hospital and St. Michael's Hospital, where he died Dec. 3, aged 77.

Miller, David Isaac, Harrisburg, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1901; an associate member of the American Medical Association; recently was named "Physician of the Year" by the Dauphin County Medical Society; formerly member of the State House of Representatives; served as medical director of Dauphin County for two terms; associated with the Harrisburg Polyclinic Hospital, where he died Dec. 14, aged 80.

Mitchell, Earl Hix Ⓜ Indianapolis, Ind.; University of Louisville (Ky.) School of Medicine, 1921; member of the American Academy of General Practice; on the staffs of the Community Hospital and the Methodist Hospital, where he died Dec. 20, aged 69.

Morris, Harold Thoes Ⓜ Topeka, Kan.; Northwestern University Medical School, Chicago, 1920; associated with Stormont-Vail Hospital and St. Francis Hospital; died Dec. 3, aged 63.

Morse, Arthur W. Ⓜ Colonel, U. S. Army, retired, Odell, Ill.; Northwestern University Medical School, Chicago, 1899; service member of the American Medical Association; veteran of the Spanish-American War and World War I; entered the regular Army in 1901 and retired Oct. 19, 1920, for disability in line of duty; died in St. James Hospital, Pontiac, Dec. 1, aged 85.

Muir, Walter Francis Ⓜ Browns Valley, Minn.; University of Minnesota Medical School, Minneapolis, 1937; veteran of World War II; associated with the Holy Trinity Hospital in Graceville and the Community Hospital; died in the University Hospitals in Minneapolis Dec. 12, aged 50.

Murray, Charles Kepharte Ⓜ Pittsburgh; University of Pittsburgh School of Medicine, 1919; fellow of the American College of Surgeons; for many years associated with the Columbia Hospital, where he died Dec. 3, aged 66.

Noble, Thomas Benjamin Ⓜ Indianapolis; Washington University School of Medicine, St. Louis, 1918; fellow of the International College of Surgeons; veteran of World War I; associated with the Community, Indianapolis General, and St. Francis hospitals; died in Laguna Beach, Calif., Dec. 8, aged 63.

Osborne, John Carlton Ⓜ Baltimore; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1942; veteran of World War II; instructor in medicine at his alma mater; on the staff of the Mercy Hospital, where he died Dec. 10, aged 42.

Riseborough, Ernest Cecil Ⓜ Detroit; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1918; associated with Warren Diagnostic Hospital; past-president of the Kiwanis Club; served as a director of the Goodwill Industries; died Dec. 3, aged 63.

Ruch, Walter Allwein Ⓜ Memphis, Tenn.; Washington University School of Medicine, St. Louis, 1928; served on the faculty of the University of Tennessee College of Medicine; specialist certified by the American Board of Obstetrics and Gynecology; member of the Central Association of Obstetricians and Gynecologists; fellow of the American College of Surgeons; served as president of the Memphis Obstetrics and Gynecology Society; on the staffs of the Methodist Hospital, St. Joseph's Hospital, John Gaston Hospital, and the Baptist Memorial Hospital, where he died Dec. 6, aged 63.

Ryan, William Patrick Ⓜ Holyoke, Mass.; University of Vermont College of Medicine, Burlington, 1911; fellow of the American College of Surgeons; veteran of World War I; held the Legion of Honor, Silver Star with Palms, and the French Croix de Guerre; director of health; associated with the Providence Hospital and the Holyoke Hospital, where he died Dec. 2, aged 72.

Smith, Jacob, New York City; Cornell University Medical College, New York City, 1920; associated with the Morrisania Hospital; died Dec. 5, aged 64.

Smith, Stuart Gross Ⓜ Major General, U. S. Army; born in Springfield, Ill., Jan. 11, 1900; Washington University School of Medicine, St. Louis, 1924; two years later accepted a commission in the medical corps reserve; graduate of the Army Medical School and the Medical Field Service School in 1927; Armed Forces Industrial College in 1939; during World War II commanded Vaughn General Hospital, Hines, Ill., before going to Europe where he served with the Civil Affairs Division of SHAEF; later commanded the 97th General Hospital in Germany; from 1946 to 1949 was commanding officer of the Armed Services Medical Procurement Agency, Brooklyn, and was assistant chief and later chief of the supply division in the office of the Army Surgeon General, Washington, D. C., from 1949 to 1951; served as surgeon of the First Army at Governors Island, N. Y., from 1951 to 1953, when he became a surgeon of the Eighth Army in Korea; returned to the United States in June, 1954, to become commanding general, Brooke Army Hospital, Fort Sam Houston, Texas, a position he held until August, 1958, when he became commanding general of Letterman Army Hospital in San Francisco; held the Distinguished Service Medal and the Commendation Ribbon with metal pendant; service member of the American Medical Association; died in the Fitzsimons Army Hospital, Denver, Nov. 19, aged 58.

Soifer, Samuel Ⓜ Forest Hills, N. Y.; born Nov. 24, 1899; University and Bellevue Hospital Medical College, New York City, 1924; specialist certified by the American Board of Urology; fellow of the International College of Surgeons; veteran of World Wars I and II; member of the Association of Military Surgeons of the United States; on the faculty of the State University of New York College of Medicine at New York City; associated with the Goldwater Memorial Hospital in New York City, Kings County Hospital in Brooklyn, and Terrace Heights Hospital in Hollis; died Dec. 4, aged 59.

Spiegel, Samuel Ⓜ New York City; Bellevue Hospital Medical College, New York City, 1898; fellow of the American College of Surgeons; on the staff of the People's Hospital; died Dec. 6, aged 81.

Steingrube, C. Roy, Cincinnati; University of Cincinnati College of Medicine, 1929; member of the Ohio State Medical Association; county health commissioner; formerly member of the county board of health; associated with the Deaconess Hospital; died Dec. 2, aged 55.

Stewart, Clinton George Ⓜ Circleville, Ohio; Rush Medical College, Chicago, 1912; served on the Pickaway County Library Board; associated with the Berger Hospital; died Nov. 1, aged 85.

Stouffer, John Franklin Ⓜ Philadelphia; Medico-Chirurgical College of Philadelphia, 1915; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association; for many years associated with the Philadelphia General Hospital; died in the Bristol (Va.) Memorial Hospital Nov. 2, aged 76.

Streysman, Francis Edward Ⓜ Oaklawn, Ill.; Loyola University School of Medicine, Chicago, 1931; police surgeon for the village of Hickory Hills; on the staff of the Holy Cross Hospital in Chicago; died Nov. 15, aged 64.

Summerville, William Eugene Ⓜ Louisville, Ky.; University of Louisville School of Medicine, 1925; member of the Southeastern Surgical Congress; served as surgeon for the Louisville and Nashville, Kentucky and Indiana Terminal, and Illinois Central railroads; on the staff of SS. Mary and Elizabeth Hospital and past chief of staff there; associated with St. Joseph Infirmary; died Nov. 11, aged 58.

Swickard, George Yeagley Ⓜ Orange, Texas; Ohio State University College of Medicine, Columbus, 1931; associated with the E. I. du Pont de Nemours and Company; member of the Industrial Medical Association; chief of the surgical staff at the Orange Memorial Hospital where he died Nov. 22, aged 52.

Thomas, Carlyle Milton Ⓜ Bangor, Pa.; Jefferson Medical College of Philadelphia, 1926; school physician in Bangor; for many years school physician; associated with St. Luke's Hospital in Bethlehem and Easton (Pa.) Hospital; died Dec. 6, aged 57.

Torrey, Eugene Weiss Ⓜ Baltimore; Jefferson Medical College of Philadelphia, 1917; service member of the American Medical Association; veteran of World War I; for many years associated with the Veterans Administration; member of the Endocrine Society and the American Psychiatric Association; died in the Veterans Administration Hospital Nov. 12, aged 65.

Van Sweringen, Walter Ⓜ Amarillo, Texas; University of Maryland School of Medicine, Baltimore, 1904; member of the Radiological Society of North America; served in France during World War I; at times on the staffs of Northwest Texas Hospital and St. Anthony's Hospital; died Nov. 16, aged 78.

Waldman, Irwin Jerome Ⓜ Milwaukee; University of Illinois College of Medicine, Chicago, 1934; service member of the American Medical Association; specialist certified by the American Board of Obstetrics and Gynecology; physician at the regional office of the Veterans Administration; died in the Milwaukee Sanitarium Foundation, Wauwatosa, Nov. 8, aged 49.

Weller, Theodore Warford Ⓜ Oakland, Calif.; Harvard Medical School, Boston, 1924; specialist certified by the American Board of Obstetrics and Gynecology; fellow of the American College of Surgeons; veteran of World War I; associated with the Samuel Merritt Hospital, Peralta Hospital, and the Providence Hospital, where he was president of the medical staff, and where he died Dec. 10, aged 64.

Wezeman, Paul Henry Ⓜ Oak Park, Ill.; Chicago College of Medicine and Surgery, 1914; for many years on the staff of the West Suburban Hospital, where he died Dec. 21, aged 75.

Whitefort, Arthur Rand Ⓜ St. Elmo, Ill.; St. Louis University School of Medicine, 1905; member of the American Academy of General Practice; served as president of the Fayette County Bank; associated with St. Anthony's Hospital in Effingham, and Fayette County Hospital in Vandalia, where he died Nov. 8, aged 78.

Williams, Christopher Smith, La Fayette, N. Y.; University of Buffalo School of Medicine, 1897; an associate member of the American Medical Association; past-president of the Syracuse Academy of Medicine and the Onondaga County Medical Society; health officer of the town of LaFayette; served on the staff of the Crouse–Irving Hospital in Syracuse; died Dec. 6, aged 86.

Wilson, Gustave Ⓜ Sacramento, Calif.; born in Stockholm, Sweden, Aug. 13, 1875; University of Michigan Homeopathic Medical School, Ann Arbor, 1903; fellow of the American College of Surgeons; past-president of the Sacramento Society for Medical Improvement; member of the California Medical Advisory Board during World War I; formerly member of the state board of health; served on the county health and welfare board, which he helped to establish; for many years a director of the Sacramento Merchants National Bank; formerly assistant superintendent of the Patton (Calif.) State Hospital; member and for many years vice-president of the board of trustees of the Sutter Hospital, where he was a member of the staff, and where he died Dec. 3, aged 83.

Wood, Harold Bacon Ⓜ Harrisburg, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1901; fellow of the American Public Health Association; at one time epidemiologist for the New York State Department of Health and the Pennsylvania Department of Health; formerly health officer of Bloomington, Ill.; served on the faculty of his alma mater; author of "Sanitation Practically Applied"; died Dec. 1, aged 80.

York, William Edward Ⓜ Giddings, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1894; died Dec. 7, aged 88.

Zeigler, Jerome Ⓜ Cincinnati; University of Cincinnati College of Medicine, 1920; member of the American Academy of General Practice; clinical instructor in medicine at the University of Cincinnati College of Medicine; member of the staff of the Bethesda Hospital, where he died Dec. 6, aged 63.

FOREIGN LETTERS

BRAZIL

Blood Groups Among Brazilian Indians.—Several studies were made of blood groups among Brazilian Indians. In the State of Paraná, Dr. L. Fernandes found that of 77 Caingangues Indians 81.6% belonged to blood group O, 13.1% to group B, and 5.3% to group A. Among 119 Bororós and 237 Caiuiás Indians in the state of Mato Grosso, Dr. L. Ribeiro and co-workers observed the same predominance of group O. More recently a study of 71 Indians living at Porto Capitão Vasconcelos in the state of Amazonas by Dr. G. M. Leite and co-workers of the University of São Paulo (*Revista paulista de medicina*, vol. 53, November, 1958) showed that all belonged to group O. The MN factors were distributed as follows: M, 46%; N, 4%; and MN, 50%. All were Rh positive.

Fungi in Gallbladder.—At the Institute of Mycology in Recife, Dr. A. C. Batista and co-workers (*Revista da Associacão médica brasileira*, vol. 4, October, 1958) found Candida and Cryptococcus in the bile of 21 of 33 patients with cholecystitis. They examined 109 samples of bile. Differences between microscopic results and the ones with culture mediums were ascribed to the use of tetracycline in the mediums to prevent bacterial growth. These findings may have a bearing on the etiology of cholelithiasis and on some allergic manifestations of unknown origin.

Asthma Treated with Hypnosis.—Dr. A. C. M. Passos, of the Escola Paulista de Medicina of São Paulo (*Revista brasileira de tuberculose*, vol. 26, December, 1958), induced hypnosis in three patients with asthma. One was treated by prolonged suggested sleep (19 hours a day) for 60 days, with excellent result. The others were treated by direct suggestion of relaxation for 30 to 60 min. They also obtained favorable results.

GERMANY

Diagnostic Errors in Bronchial Carcinoma.—In some patients it is difficult to diagnose bronchial carcinoma correctly, especially early in the course of the disease. For this reason an exploratory thoracotomy is often necessary. Becker and Knothe (*Thoraxchirurgie* **6**:235, 1958) investigated a series of 443 patients who were subjected to thoracotomy and whose conditions had been diagnosed as bronchial carcinoma at the surgical clinic of Giessen University. There were 18 diagnostic errors among 256 resections (7.1%) and 4 among 190 thoracotomies (2.1%). Ten patients had chronic pneumonitis, six tuberculosis, three a benign bronchial tumor, one Hodgkin's disease, and in two the diagnosis could not be determined. As most of these conditions required surgical treatment little harm was done by performing the thoracotomy, but in some of the patients a correct diagnosis would have prevented resection of a whole lobe. In six patients the wrong diagnosis was due to preoperative and/or intraoperative histological examination. In many cases the cause of histological diagnostic errors was that too little material was obtained for examination. Because of these diagnostic errors, sputum examination and/or bronchoscopy are no longer relied on and a pulmonary biopsy specimen should be obtained for final verification of the diagnosis.

Isoniazid Resistance.—Along with the decrease in mortality from pulmonary tuberculosis, an increase in the number of incurable cases of open tuberculosis has been noted. To reduce the risk that such patients constitute as potential sources of infection, it is necessary to expand control programs insofar as possible. The possibility of reducing the virulence of the Mycobacterium tuberculosis discharged by these people is being explored. The virulence of highly isoniazid-resistant tubercle bacilli is usually greatly diminished. H. Bierschenk (*Ztschr. Tuberk.* **111**:159, 1958) reporting on a study of 37 patients with open tuberculosis, 13 of whom had tubercle bacilli of normal sensitivity in their sputums, concluded that isoniazid-resistant tubercle bacilli rarely cause disease unless the infecting dose is extremely high or the patient is particularly susceptible. Continuous administration of isoniazid reduces the danger of the nonisolated patient with open incurable tuberculosis as a source of infection. The time required and degree of the decrease of infectivity cannot be predicted but the time is probably several months.

Cancer in Childhood.—Among the causes of death in childhood, infectious diseases have ceased to predominate. Fatal accidents now hold first place. They are followed in order of frequency, in all civilized countries, by malignant disease, including leukemia, lymphosarcomatoses, carcinoma, and sarcoma. In the state of North Rhine–Westphalia, the number of deaths from malignant disease has

The items in these letters are contributed by regular correspondents in the various foreign countries.

superseded that from tuberculosis. In children aged 6 to 15 malignant disease ranks higher than pneumonia and tuberculosis combined. In the whole Federal Republic, this marked increase in mortality from tumors and leukemia has been observed among infants and children since 1951. It is only partly relative, i. e., explained by the decreasing mortality from infectious diseases. E. F. Hugh (*Ärztl. Wschr.* 13:990, 1958) surveyed the tumor localizations of patients at the children's clinic of the medical academy at Düsseldorf and found in the order of descending frequency: leukemia and tumors of the brain, kidney, soft tissues, eye, and bones. Some of the most frequent tumors of children were distinguished from those of adults by being genuinely embryonal. Preventive measures recommended include the exclusion of all carcinogenic agents from both mother and child, and avoidance of exposure of infants to x-rays. It is not sensible to protect the fetus in utero from x-rays only to expose the infant after birth to unnecessary radiologic examinations.

INDIA

Lung Surgery.—P. Singh (*Indian Journal of Surgery*, vol. 20, October, 1958) analyzed a series of 238 patients subjected to lung surgery. In most of them the pulse rate was well stabilized preoperatively. A few because of a high pulse rate had to be operated on in two stages at an interval of two to three days and did well even when the preoperative pulse rate was 100 to 140. Some had a high temperature at the time of operation and these were also operated on in two stages. Breath-holding time was another preoperative criterion, a patient with a breath-holding time of 45 seconds or more being considered an excellent risk; one with 30 to 45 seconds, a good risk; and one with less than 30 seconds, a poor risk. Patients with a breath-holding time of over 30 seconds and vital capacity of over 2 liters usually behaved well during the operation. An exercise tolerance test was made on 37 patients and served as a useful guide to physical status. A hemoglobin level of 10 to 15 Gm. was considered favorable, although occasionally patients with lower values had to be operated on. Most of the patients before operation had a sedimentation rate of less than 20 mm.

In most patients anesthesia was induced with thiopental and maintained with nitrous oxide, oxygen, and ether. Tracheal obstruction by secretions was not common as most of the patients were well prepared by regular postural drainage but some required bronchoscopic aspiration before anesthesia. Postoperative complications, besides shock and hemorrhage, included subcutaneous emphysema, mediastinal emphysema, pneumothorax, contralateral spontaneous pneumothorax, mediastinal displacement, paradoxical respiration, tachycardia, arrhythmias, retained secretions, pulmonary edema, atelectasis, laryngotracheal bronchitis, pulmonary infections, hydrothorax, and acute dilatation of the stomach. There were 10 deaths in the series, 7 due to shock, 1 due to anuria, and 2 unexplained.

Sulfamethoxypyridazine.—P. G. Kamath and coworkers (*Indian Journal of Medical Sciences*, vol. 12, November, 1958) treated 28 patients who had acute urinary and respiratory tract infections with sulfamethoxypyridazine, a long-acting sulfonamide. Only those who were not previously treated by other sulfonamides or antibiotics were included. The drug was given orally, the common dosage schedule being 1 Gm. as initial dose, followed by 0.5 Gm. daily. In severe cases 2 Gm. was given initially, followed by 1 Gm. daily. The larger dosage was also used when there was no response to the lower dosage within two or three days. The duration of treatment varied from 4 to 16 days. A good response was observed in 21, a poor or no response in 3, and in 4 the drug had to be discontinued because of toxic effects. The series included 15 patients with lobar pneumonia, 12 of whom showed a good response. The fever subsided on an average within 32 hours and the cough and pain in the chest subsided within three or four days. Of the three who failed to respond, two developed acute mania, one on the second day and one on the third day, and one developed hemorrhage and oliguria. There were six patients with bronchitis, all of whom showed a good response. One patient in this group complained of mild headache.

Of the four patients who had urinary tract infection with Escherichia coli or Proteus vulgaris, only one patient suffering from pyelitis due to P. vulgaris responded to the drug, the fever subsiding in six days and the pyuria showing a decrease. The urine cleared completely after 14 days, at which time urine culture was negative. The other three showed no improvement even after administration of the drug for 12 days. Of the remaining three patients one had a congenital cystic lung, one bronchiectasis, and one bacillary dysentery. The last two responded well but the first, after an initial improvement, developed acute delirium on the third day and this form of treatment was stopped. The clinical results of this drug in infections of respiratory tract were comparable to those with sulfadiazine. The number of pneumonia patients developing psychosis during treatment was, however, alarming.

Parekh and Adiga in the same journal reported the use of this drug in a series of 84 patients and 40 normal controls. Eight of the patients developed psychotic manifestations but the severity of infection could not be held responsible for these symptoms. Two had received only small doses of the drug and the duration of therapy was short.

Ony one patient gave a family history of mental illness. The toxic effects were attributed to the presence of a pyridine and a methyl group in the drug and the occurrence of psychosis in none of the controls suggested the possibility of the anoxia occurring in pneumonia having some relation to the toxicity of the drug.

Bone and Joint Lesions in Smallpox.—The *Indian Journal of Surgery* (vol. 20, October, 1958) contained a study of 10 subacute cases of smallpox arthritis uncomplicated by sinus formation. Biopsies of bone, muscle, joint capsule, and synovial membrane were performed to determine the kind of lesions present. Fluid aspirated from the joints was cultured. Clinically these cases resembled those of pyogenic arthritis except for absence of fever. Bilateral involvement and affection of elbow joints were common findings. Cases coming one to two years after the attack of smallpox showed fibrous ankylosis, and those coming seven or eight years later showed disturbances of growth, although there was a surprising amount of movement in the affected parts. Bony ankylosis occurred only if there was secondary infection after sinus formation.

The radiologic features in the subacute stage resembled those of chronic pyogenic arthritis except that both contiguous ends of the bones forming the joint were involved. Cystic changes and subperiosteal bone formation without sequestrums and without marked necrosis and new bone formation were characteristic features. Both epiphysis and metaphysis were involved along with the joint, and isolated bone involvement was rare. Joint changes consisted of increase in joint space and erosion of articular ends with some periarticular soft tissue swelling. In late cases the joint space was diminished with deformed articular ends, and, in some, scalloped ends with widening of the joint space was noticed.

Cultures of aspirated material and of tissues removed at biopsy were sterile. The microscopic appearance of the bone resembled that of osteitis fibrosa with occasional round cell infiltration. Soft tissues such as muscle, synovial membrane, and fascia showed fibrosis, hemorrhage, and round cell infiltration. The purely osseous lesions improved with scraping and curettage. Partial excision was performed in the osteoarticular type when satisfactory movement was obtained in the elbow in one patient and in another this operation was a failure. Nonspecific protein therapy and active use in a late case caused improvement in the range of movement. Eight early cases with swollen and tense joints improved with splinting and rest. One patient with bony ankylosis was subjected to manipulation under anesthesia to improve the angle of ankylosis. During follow-up study of these cases, a gradual improvement in the range of movements without any recurrence of inflammation was noticed. Deformities due to epiphysial damage tended to increase during the growth period requiring osteotomy in one patient for correction of valgus deformity at the knee joint.

Auxiliary Nursing.—A brighter future for the auxiliary nurse and better training for this type of health worker were called for at the 12-nation conference of auxiliary nursing sponsored by World Health Organization in December in New Delhi. It was suggested that local nursing school committees be set up to meet the needs of health services by improving local recruitment. The main purpose of such committees would be to inform the public about nursing training and services and to make living and service conditions of nursing workers attractive. At ministry level a nursing board or council would be able to encourage recruitment in the state or country as a whole. One group suggested that the registration of auxiliary nurses was desirable. Every auxiliary nurse should receive basic training to prepare her to act as an assistant nurse. Such assistant nurses could be employed in institutions where day-to-day supervision by trained nurses was available. For workers to be assigned to such specialized fields as tuberculosis, a further period of training would be necessary.

Health Aspects of Radiation.—A new step towards establishing India as a training center for southeastern Asian workers in the health aspects of radiation and atomic energy was taken in November when about 20 students from three southeastern Asian countries began a five-week course in health physics in Bombay. There were also four participants from the western Pacific region. This course is designed for physicists who will serve as supervisors and instructors in radiation protection. It is sponsored by the Indian Department of Atomic Energy and the World Health Organization with the cooperation of the Atomic Energy Commission of the United States.

Fractures of the Neck of the Femur.—Bhansali and Dholakia treated 30 patients with fracture of the true neck of the femur, their ages varying from just below 20 to 80 years. Three had valgus and 27 had varus fractures. The injury responsible for most of the fractures was an accidental fall while walking, running, or alighting from a train. The method of treatment depended on the type of fracture as seen radiologically, the duration of the fracture, the presence or absence of complications, the age of the patient, and the economic circumstances. The three patients with the valgus fractures were treated with simple bed rest, the limb being kept in a neutral position with the help of sandbags for three months. Smith-Peterson nailing was performed in 16 patients, in 5 of whom secondary operations were required. The shortest time between injury and

operation was 2 and the longest 30 days. A plaster boot with a wooden board incorporated in its posterior part was applied immediately after the nailing to keep the limb in a position of internal rotation. Antibiotics were given routinely to all patients. Static quadriceps exercises were started on the same day or the next. On the third day the knee on the affected side was moved after turning the patient on the sound side. The patient was made to sit up in bed on the 4th or 5th day and the plaster boot was removed on the 12th to 14th day. Weight-bearing on the affected side was not allowed till there was radiologic evidence of sound bony union. There were three deaths in this series.

Fibrocongestive Splenomegaly.—Goyal and Gupta (*Current Medical Practice*, vol. 2, November, 1958) stated that the cause of Banti's disease is still controversial. Such factors as portal hypertension, chronic intoxication, and allergy have been considered. The authors studied the role of allergy in patients and experimental animals. Of 100 specimens from spleens removed at operation or autopsy, 37 showed the lesions of malaria, 30 formed a miscellaneous group, in 15 the enlargement was due to congestive heart failure, 13 showed varying degrees of fibrosis and congestion, and 5 showed the lesions of tropical splenomegaly. Spleens weighing 150 Gm. or more and showing evidence of fibrosis and congestion were classified as cases of Banti's disease. The liver and portal veins could be examined in 13 cases and only 6 of these showed evidence of portal obstruction; 2 were due to right-sided failure and 5 were from patients with such infections as bronchiectasis and tuberculosis. Thus all the cases of Banti's disease were not due to portal obstruction.

To determine the role of allergy in causing fibrocongestive splenomegaly, repeated injections of sheep serum were given to rabbits and repeated injections of tuberculin were given to a series of guinea pigs rendered allergic by previous injection of BCG vaccine. No splenomegaly developed in the rabbits although all spleens in rabbits that were killed from the 10th week onward showed fairly marked congestion and fibrosis. The spleen in guinea pigs also showed no enlargement, but there was microscopic evidence of congestion and a certain degree of reticuloendothelial hyperplasia with presence of hemosiderin in macrophages and extracellularly. Fibrosis was evident seven weeks after the commencement of the tuberculin injections. Thus allergy probably played some part although absence of marked enlargement indicated that it alone could not be responsible when there was no portal obstruction.

Surgical Ascariasis.—A. E. deSa (*Indian Journal of Child Health*, vol. 7, November, 1958) reported a series of 43 cases of roundworm obstruction in children. Surgical ascariasis was found to be the second largest cause of intestinal obstruction in children, the first being imperforate anus. The age of these patients varied between 2 and 10 years. Abdominal pain, vomiting, constipation, and fever were the most frequent symptoms, others being distention, drowsiness, and roundworms in vomitus and stools. The three most frequent signs of ascarideal obstruction in this series were the presence of a palpable and occasionally a visible mass, fever, and toxemia. The roundworm mass tended to be central, migrating from one part of the abdomen to another and frequently breaking up into two or more masses. The toxemia closely resembled that of typhoid with apathy, delirium, and muscular twitching. This was often dramatically relieved by intravenous administration of 25 cc. of 50% dextrose solution. The fever rarely exceeded 101 F (38.33 C). Increase in the eosinophilic count was not a reliable diagnostic sign.

Of the four types of obstruction attributed to ascaris (mechanical, spastic, ascarideal intussusception, and ascarideal volvulus), only the first two were observed in this series. There was only one case of spastic obstruction among the patients operated on, the walls of the ileum being powerfully contracted on a roundworm lying longitudinally inside so as to produce marked obstruction. The obstruction was commonly due to a firmly packed bolus of worms with the antimesenteric border showing areas of ischemia and gangrene when the lump was big. Proximal distention was never as pronounced as in other organic intestinal obstructions.

In one child a large number of the roundworms had found their way into the general peritoneal cavity through a pinpoint opening in the tip of the appendix, while in another no perforation was found in any part of the gastrointestinal tract, but the general peritoneal cavity was full of worms. Neither patient showed any peritoneal reaction, the edges of the perforation in the former being smooth, bleeding readily, and free of any fibrinous deposits. A chronic intraperitoneal abscess was occasionally seen after an indolent roundworm perforation. Thus one patient was brought in because of a liver abscess, the live roundworm wriggling out of the drainage opening after incision.

The author favored conservative treatment of these patients with operation only when the diagnosis is in doubt, perforation is diagnosed or suspected, distention is pronounced and progressive, or when conservative management has failed to relieve the distention and the general condition deteriorates. Conservative management includes correction of fluid and electrolyte imbalance by parenteral fluid administration, continuous gastric suction, daily saline enema, administration of atropine to counteract spasm, intravenous infusion

of 25% dextrose solution for the toxemia and the administration of specific anthelmintics and suitable antibiotics. Of the 34 patients who were treated conservatively 28 were given santonin and calomel at night, followed by a simple enema next morning and a small dose of magnesium sulphate if it was found to be safe. This treatment was repeated once in one case and twice in another; six patients were given hetrazan syrup. The roundworms were generally passed within 24 hours and no purgation was required. The fact that purgation was not necessary with hetrazan as with santonin was a distinct advantage. In two patients the roundworms were passed soon after an intramuscular injection of 0.3 or 0.4 mg. of atropine. Penicillin and streptomycin were given routinely to combat associated infection. Six patients were operated on, three of whom died. Of the 34 treated conservatively, six died. In a patient with Meckel's diverticulum with a band obstruction roundworms crawled out of the umbilicus. This patient was operated on and died. The author stressed the inadvisability of early operation as most patients respond to conservative treatment.

Family Planning Program.—The Family Board requested that a tentative provision of $2,100,000 be made by the Government of India for the implementation of the Family Planning Program during the fiscal year 1959-1960. The main feature of this program would be an intensification of training and educational schemes, opening and maintenance of clinics, appointment of family planning education leaders, holding of orientation camps, free distribution of contraceptives through all primary health centers and medical institutions, strengthening of the institutions, and strengthening of the inspection organization and research. The number of clinics so far opened is 718. Against the target of 150 urban and 600 rural clinics by March, 1959, 171 urban and 400 rural clinics have been started. The state governments hope to open 151 additional rural clinics before March.

Leprosy.—Kelkar and Randive (*Indian Journal of Medical Sciences*, vol. 12, November, 1958) stated that many unsuccessful attempts have been made to transmit human leprosy to laboratory animals. They studied the role of such factors as age, repeated contact, and general resistance. Because children are known to be more susceptible to the disease than adults, newborn animals (75 rats, 36 hamsters, and 24 mice) were given multiple inoculations of human lepromatous material. The general resistance is on an average low in the tropics and subtropics where this disease is common. The body resistance of the laboratory animals was lowered by giving cortisone, feeding a diet deficient in vitamin B_1, sensitization with lepromin, administration of hyaluronidase, and exposure to x-rays. The inoculum consisted of a human lepromatous nodule and a suspension of human lepra bacilli. The nodule was inoculated subcutaneously and the suspension intramuscularly or intraperitoneally. Young adult rats thus inoculated served as controls. Both the groups were observed for 8 to 18 months.

The hamsters, 7 of which served as controls, were treated with varying doses of x-ray. Both the groups were observed for six months and killed when the animals looked emaciated. Of the 75 rats, 42 showed acid-fast granules in their tissue cells and a nonspecific cellular reaction which was mainly of a defensive inflammatory nature. The few organisms seen were in and around nerves, and a large number of acid-fast granules were seen in macrophages with diffuse pink cytoplasm. The control rats and those treated with cortisone and a vitamin B_1-deficient diet did not show any significant difference in their tissue reaction to repeated inoculation of human lepromatous material. The reaction, however, was more pronounced and a larger number of animals was affected when cortisone and a vitamin B_1-deficiency diet was given prior to inoculation.

The intraperitoneal inoculation of human lepra bacilli was found to be more effective than inoculation by any other route. There was a complete absence of tissue reaction in the mice treated with hyaluronidase or lepromin prior to inoculation. A study of tissue reactions in the hamsters showed evidence of survival, maintenance, and even proliferation of acid-fast organisms in over 50% of those in the irradiated group. Such evidence was absent in those treated with cortisone and in the controls. In young hamsters showing evidence of disease, the bacilli were liberated into the subcutaneous tissue after disintegration of the transplanted lepromatous nodule. Some bacilli were ingested by macrophages and others transported to regional axillary lymph nodes via lymphatics where they were again engulfed by macrophages and other cells of the reticuloendithelial system. The older hamsters so treated showed marked tissue damage. The tissue reactions suggested a progressive generalized infection. A dose of 100 r whole body irradiation given to young adult hamsters prior to inoculation of lepra bacilli thus proved to be a means of lowering body resistance of these animals to leprosy.

Anemia and Kwashiorkor.—Ismail and Chandra (*Indian Journal of Child Health*, vol. 7, November, 1958) treated 50 patients who had iron-deficiency anemia with intramuscular injections of an iron-dextran complex. These patients were divided into those in whom the iron deficiency was not associated with kwashiorkor (30) and those who had both conditions (20). The total dosage of elemental iron ranged from 700 to 1,200 mg. A 22-gauge needle of sufficient length to penetrate well beyond

the superficial tissues and fat layers was used so as to ensure that the pool of iron was placed deeply into the muscle and to prevent it from leaking back into the subcutaneous tissues. The patients showed the usual clinical features of iron-deficiency anemia but koilonychia was rare. Glossitis, pigmentation, and dysphagia were also uncommon. In the first group 25 patients had a history of malnutrition, 13 of ascariasis, 8 of malaria, and 13 of repeated attacks of diarrhea. Three had active tuberculosis, one with tuberculous meningitis; seven had other respiratory infections, two urinary infections, and four hookworm infestation. In the second group 16 had a history of malnutrition, 12 of ascariasis, 8 of malaria, and 17 of repeated attacks of diarrhea. Two had tuberculosis and five had other respiratory infections. No patient was below one year of age.

The initial hemoglobin level in the first group varied from 20 to 50%. The average rise in the first week was 10% while over a four-week period the maximum rise was 60% and the minimum 10%. In the second group the initial hemoglobin level was 20 to 60% and the average rise during the first week was 8%, the maximum response being 30%. The red blood cell counts varied from 1.5 to 3 million in the first group and showed an average rise of 1.5 million in four weeks. The erythrocyte count and the PCV rose more rapidly than the hemoglobin level. In the second group, the initial erythrocyte count varied from 1 to 3.5 million and rose by 1.25 million after four weeks. Macrocytes and target cells were seen in the blood smears in many patients, indicating that the anemia in kwashiorkor may be of a mixed type. The bone marrow in the first group was typical of microcytic anemia with normoblastic reaction and in the second group the findings were those of a macronormoblastic reaction without any megaloblasts. The initial serum iron level showed great variation, the mean value being 50 mcg. per 100 ml.

After treatment, serum iron levels of 64 to 400 mcg. per 100 ml. and above were recorded. The total plasma proteins were low in both groups and the albumin/globulin ratio was altered. These changes were more marked in the second group but they were not related to the clinical features of the kwashiorkor or the severity of the anemia. Toxic reactions and local side-effects were almost absent. No allergic or pyrogenic reactions occurred. The advantages over oral iron therapy were that the absorption was not limited by the activity of the mucosal barrier, there was no likelihood of the treatment being suddenly discontinued, and a known quantity of iron could be given ensuring a rapid response.

Typhoid in Children.—Paul and Jatkar (*Indian Journal of Child Health*, vol. 7, November, 1958) found that of 2,000 admissions to the K. S. Children's Hospital, New Delhi, over a period of 21 months, 56 were for typhoid. Only two of these patients were between 1 and 2 years old. The highest incidence was between 5 and 9. The greatest number of cases were seen in June, July, and August. Two patients had had triple typhoid vaccination 1 and 2 years, respectively, prior to admission. A history of contact was available in six patients. The temperature did not follow any particular pattern, high, moderate, and low remittent grades being commoner than intermittent. Blood cultures positive for Salmonella typhosa were obtained in 37 cases. The Widal test was positive in titers of 1:60 to 1:3,200 in 25 patients. This test was not run on all patients with positive blood cultures and some who had positive blood cultures did not show a rise in titer.

The leukocyte count varied from a marked leukopenia to leukocytosis. A normal count was restored in those with leukopenia after treatment with chloramphenicol. The polymorphonuclear count varied from 40 to 80%. Three patients suffered a relapse which responded to a second course of chloramphenicol. There were four deaths, one due to encephalopathy, one to hepatitis, one to bronchopneumonia, and one to uncontrolled diarrhea. A full diet was given as soon as possible, usually within two or three days of admission, when the toxemia and fever abated. Three consecutive negative stool cultures at weekly intervals were considered necessary before discharging the patient. Typhoid fever is so common in India that it must be considered in all patients whose fever lasts more than three days.

Meprobamate in Tetanus.—Damany and Kamat (*Journal of the Indian Medical Association*, vol. 31, Nov. 16, 1958) stated that a fully conscious mind with the painful awareness of spasms probably increases the frequency of spasms and rigidity in tetanus. Tranquilization has therefore been considered essential in the treatment of this disease. The centrally acting sedatives commonly used have the danger of producing central depression. None of the muscle relaxants acting peripherally have proved uniformly successful and some of them also give rise to dangerous side-effects such as hemoglobinuria and pulmonary edema.

The authors therefore studied the usefulness of meprobamate which has both muscle relaxing and ataratic action, is orally effective, and has low toxicity. In their series of 66 patients with tetanus, 27 received the usual treatment with tetanus antitoxin, antibiotics, and sedation, and 39 received meprobamate in addition. The drug was given orally in six hourly doses of 800 mg. in adults till cure or death occurred. It was omitted temporarily in those who showed complications. Patients with a period of onset of spasms of less than 24 hours showed a higher mortality in both groups (50% in

the first group and 33% in the second) than those with the period of onset longer than 24 hours (19.1% in the first group and 18.5% in the second).

The duration of stay in hospital of those who survived varied from 8 to 26 days in both groups. Death in most of those who died occurred within 48 hours of admission. The percentage survival rate was a little better in the second group than in the first but meprobamate did not alter the course of the disease significantly. Whatever beneficial influence it had was seen only in mild and moderate types of cases, while the severer type was unaffected. Its tranquilizing and muscle relaxing action was apparently not strong enough to control the spasms and rigidity of tetanus. Another disadvantage was the prolonged period before its effects became manifest. No serious side-effects were attributed to the drug.

SWEDEN

Basophils in Asthma, Dermatitis, and Psoriasis.—The average basophil count in the peripheral blood of 20 patients with asthma, 30 with atopic dermatitis, and 22 with nonerythrodermic psoriasis was studied by Hans Rorsman (*Acta dermat.-venereol.* **38**:175, 1958) to determine whether the decrease of basophils observed in urticaria was characteristic of allergic diseases or diseases of the skin. The control group consisted of 96 normal persons. None of the patients had an average count which significantly differed from the mean count of 44.8 ± 2.4 per cubic millimeter in the controls, but 5 patients with exfoliative erythroderma had an average of 95.6 basophils per cubic millimeter (range 42 to 214).

Exposure of Ruptured Lumbar Disks.—Carl Hirsch (*Acta orthop. scandinav.* **28**:76, 1958) stated that hypotension keeps bleeding under control while disk surgery is in progress and offers a good view of the exposed area. It also protects against postoperative hematoma. This approach should limit the damage to important functional elements. By making the incision in the dorsal fascia lateral to the spinous processes and closing the wound with the spine flexed, postoperative tightness is less pronounced. Extensive disk removal protects against disk material being squeezed out when early weight-bearing is permitted. The patient is allowed out of bed after the operation. No physiotherapy, no support, and no fusion are needed.

Oxygen Saturation of the Cord Blood.—The oxygen saturation in the blood of the umbilical cord was measured with the Brinkman Haemoreflektor in 90 cases of cesarean section, of which 16 were classified as complicated and 74 as uncomplicated by Sjöstedt and Rooth (*Acta anæsth. scandinav.* **2**:99, 1958). In uncomplicated cases in patients delivered under local anesthesia before the onset of pains, the oxygen saturation in the vein was 62.1%, and in the arteries 32.4%, i. e., the same values as in uncomplicated spontaneous deliveries. With the onset of pains the oxygen saturation decreased. Inhalation anesthesia with cyclopropane resulted in a marked depression of the oxygen saturation of the fetal blood and diminished the arteriovenous difference in the oxygen saturation, which led the authors to conclude that when local anesthesia can be used without risk to the mother this method is best for the infant.

Adrenocortical Hyperplasia.—A family consisting of normal parents, three healthy children, and three children with congenital hyperplasia of the adrenal cortex was studied clinically and analyses of their steroid excretion were made by G. Birke and coworkers (*Acta endocrinol.* **29**:55, 1958). The parents and the three healthy children exhibited a normal excretion pattern of all steroid groups studied. One of the three affected children died at the age of 8 weeks before any steroid analysis could be undertaken. The other two children with adrenocortical hyperplasia showed a substantially increased excretion of both 17-ketosteroids and 17-hydroxycorticosteroids and pathologically altered excretion patterns. Of the individual 17-ketosteroids, androsterone was predominant and little, of any, etiocholanolone could be found. Of the individual 11-oxygenated 17-ketosteroids, 11-ketoandrosterone and 11β-hydroxyandrosterone were isolated and identified by infrared spectroscopy; 11-hydroxyetiocholanolone could not be detected. An indirect analysis of the 17-hydroxycorticosteroid pattern revealed the presence of huge amounts of pregnanetriol. Measurable amounts of tetrahydro-17α-hydroxycortexone tetrahydro-S) were also demonstrated in the urine. In neither of the two children was the excretion of the latter accompanied by hypertension. Tetrahydrocortisone and 11-ketopregnanetriol or cortolone were also identified, but no 11β-hydroxylated corticosteroids could be detected. The preoperative estrogen pattern was characterized in both patients by the complete absence of estriol. After bilateral adrenalectomy substantial amounts of estriol were detected in the urine in the case of a female pseudohermaphrodite, aged 15, with adrenocortical hyperplasia treated first by excision of the clitoris, then by bilateral subtotal adrenalectomy when cortisone in the dosage required for suppressing the adrenocortical secretion gave rise to mental symptoms.

Treatment of Salicylate Intoxications.—Celander and Haglund (*Acta anæsth. scandinav.* **2**:123, 1958) used a combination of neuromuscular block, artificial respiration, and fluid and electrolyte therapy to treat severe salicylate intoxication. Of 20 pa-

tients treated 15 were under 6 years of age. A liberal supply of fluid and calories in the form of an intravenous dextrose solution was given while further clinical and laboratory analyses were being made. Controlled respiration combined with neuromuscular block when respiratory failure threatened was essential. Tubocurarine was used as the neuromuscular blocking agent. Tracheotomy was performed and artificial respiration maintained with the Gothia respirator. In no case was respirator treatment necessary for more than two days. During that time, the patient was allowed the necessary muscular rest, the acid-base disturbances were corrected, and salicylate excretion was achieved.

Myocardial Infarction.—Gunnar Biörck and coworkers (*Acta med. scandinav.* **162**:81, 1958) made a follow-up study of 903 patients who were discharged from Malmö General Hospital after a myocardial infarction. The follow-up group represented 92.7% of those who were discharged home from a total of 1,530 patients hospitalized between 1935 and 1954. These patients were divided into 389 followed for more than five years, 246 followed for two to five years, and 268 followed for two years or less. Of the total series 63% survived a further 5 years, and 40% a further 10 years. If the acute mortality is included, the chance of a 5-year survival at the moment of hospitalization was 39%, and the chance of a 10-year survival was 23%. The survival rate decreases with increasing age at the moment of infarction, but in comparison to sex-age-specific death rates in the population, the prognosis for younger persons was worse than the prognosis for older people. There was a slight general tendency toward a better prognosis for the patients discharged in the latter part of the period investigated. This change was much smaller than the decrease in acute hospital mortality.

There was no obvious sex difference in the material, but in comparison to the sex-age-specific death rates of the population at large, there might be a slightly worse long-term prognosis for women in the ages over 60, which was, however, not statistically significant in the patients reported on. The prognosis for patients with a more severe infarct was not definitely worse than that for those with a mild infarct. Hypertension did not seem to affect the long-term prognosis. Patients with diabetes had a worse long-term prognosis than those without diabetes. Anticoagulant therapy during the acute stage of the infarct did not influence the long-term prognosis, but the interpretation of that finding must be guarded. There was some uncertainty connected with death certification, and while no detailed conclusions were made by the authors, they listed 41.9% dead of subsequent myocardial infarction, 31.9% of coronary heart disease with no evidence of acute myocardial infarction, 6.7% of cerebrovascular diseases, 9.0% of other cardiovascular diseases with 3.7% as malignancy, and 6.7% as miscellaneous for a total of 489 patients for whom such records were available.

Physical Work and Mitral Valvular Disease.—The physical working capacity and its relationships to heart volume, total amount of hemoglobin, and stroke volume was studied in 42 patients with mitral valvular disease, of whom 39 had isolated or predominant mitral stenosis and 3 had isolated or predominant mitral regurgitation. Operation was performed on 27 patients. The physical working capacity, estimated as the work performed continuously at a pulse rate of 170 per minute, was directly correlated to the stroke volume during work. In mitral stenosis the heart volume was large and the working capacity low in relation to the total amount of hemoglobin. A marked enlargement of the heart was usually combined with a high pulmonary vascular resistance. In some patients, however, in whom the pulmonary resistance was almost normal the enlargement might be partly due to left myocardial insufficiency. The degree of incapacity as judged from the exercise tolerance test showed good correlation to the degree of the hemodynamic disturbances. In the patients with mitral regurgitation the heart volume was large but the working capacity normal in relation to the total amount of hemoglobin and the pulmonary vascular resistance was normal, as reported by A. Holmgren and coworkers (*Acta med. scandinav.* **162**:99, 1958).

Ulcerative Colitis and Cirrhosis of the Liver.—Ten patients who had ulcerative colitis with coexistent cirrhosis of the liver were reported by Lill Olhagen (*Acta med. scandinav.* **162**:143, 1958). In eight, signs of cirrhosis preceded the ulcerative colitis or became manifest so early in the course of the colonic disorder that the condition could not have been the cause of the cirrhosis. Signs of portal hypertension were present in every instance. In view of the disappearance of intestinal symptoms after lienorenal anastomosis in two, it seemed likely that the portal stasis might have caused the ulcerative colitis. Mucosal changes in the colon might be brought about by long-standing venous stasis in the intestine leading to anoxia and impaired nutrition of the mucosa, a mechanism similar to that underlying the formation of varicose ulcers of the leg. No evidence of a causal connection between the two conditions could be shown and until wider experience is gained of operations designed to relieve portal stasis, the presence of ulcerative colitis strengthens rather than weakens the indications for operation.

Physiological Studies of Laborers.—Irma Åstrand (*Acta med. scandinav.* **162**:155, 1958) examined 81 truck drivers at rest and during work; 12% had pathological or suspected pathological electrocardiographic tracings at rest and 19% had pathological

and 33% suspected pathological tracings during work; 32% had high blood pressure at rest and 47% were considered as overweight. The vital capacity averaged 4.64 liters and the residual volume 1.99 liters or 30% of the total capacity. The ventilation per liter of oxygen intake at submaximal work was about 4 liters higher than for younger persons. The maximal pulmonary ventilation was, however, much lower; 72 of the subjects performed heavy muscular work and of these 2 had cramp-like pains in the precordium as the most troublesome symptom; 20 complained of dyspnea, 31 of local muscular fatigue, 6 of pains in the knee or hip, and the remaining 13 complained of being tired without any specific symptoms. None of the above-mentioned findings were highly correlated with maximal oxygen intake or maximal heart rate. The reason for the decreased physical work capacity could not be explained.

Diabetes and Portal Cirrhosis.—The case records from 108 patients with cirrhosis of the liver (67 men and 41 women) were reviewed by Ragnar Hed (*Acta med. scandinav.* **162**:189, 1958) with particular attention to the presence of diabetes. The diagnosis of cirrhosis was verified in all cases at autopsy or by liver biopsy. Chronic alcoholism was present in 55.2% of the men and 4.8% of the women. Primary carcinoma of the liver was present in 20.9% of the men at autopsy and in 4.8% of the women. Diabetes was definitely present in 18 cases (12 men and 6 women). The diabetic incidence was 14.3% in the women and 17.6% in the men. Since these figures were higher than those for diabetes in the entire autopsy material during the same period, a relationship between cirrhosis of the liver and diabetes was assumed to exist. In seven further cases (six men and one woman) the fasting blood sugar level was significantly elevated. If these patients were included, the incidence of impaired sugar metabolism of diabetogenous type becomes 26.5% for the men and 16.7% for the women. The type of diabetes present in this series was comparable to that usually appearing first at from 40 to 60 years of age and occurring most commonly in women. In the present series, however, the diabetic incidence was higher in the men. In explanation of this phenomenon the author suggested that alcoholic cirrhosis was more frequently associated with impairment of carbohydrate metabolism of diabetogenous type than were other forms of cirrhosis.

Carbohydrate Metabolism in Chronic Alcoholism.—A series of 75 male alcoholics was investigated with a view to determining the incidence of disturbances of carbohydrate metabolism by Ragner Hed (*Acta med. scandinav.* **162**:195, 1958). In 24 glucose and insulin tolerance tests and liver biopsy were done. Diabetogenous disorders of sugar metabolism were demonstrated in 12 of these, of which 10 showed cirrhosis and 2 a high-grade fatty liver. Four of these 12 patients had manifest diabetes and 8 only diabetogenous glucose tolerance curves. In many of these 8 patients the fasting blood sugar was also pathologically elevated on several occasions. In the intravenous insulin tolerance test relative insulin resistance was demonstrated in all 12. The results of the investigations in these 12 patients indicated a difference in degree only with respect to the diabetogenous sugar metabolism disturbance between the 4 with manifest diabetes and the 8 with only diabetogenous glucose tolerance curves. In 12 patients the glucose tolerance curves were of the nondiabetogenous type. In the intravenous insulin tolerance test the hypoglycemia appeared within the normal interval in all 12 patients. None of these had fully developed cirrhosis. Two types of hypoglycemia were observed—a transient form associated with an alcoholic debauch and a more chronic form. In the present series hypoglycemia was associated with the milder cases of liver degeneration and diabetogenous metabolic disorders in the patients with more pronounced hepatic lesions.

Cardiac Changes in Chronic Alcoholism.—Frederiksen and Hed (*Acta med. scandinav.* **162**:203, 1958) made electrocardiograms of 121 male alcoholics aged from 20 to 40 years. In no case was hypertonia, vitium cordis, thyrotoxicosis, or inflammatory cardiac disease present. In 66 the ECG was entirely normal. In 36 the only abnormality was tachycardia above 95 per minute. In 19 others electrocardiographic changes were found as well. Four patients showed auricular fibrillation. In addition, three presented broad, notched P waves, which were also interpreted as due to auricular lesions. It therefore seemed conceivable that the auricle was one of the sites of predilection for cardiac lesions in chronic alcoholism. Isoelectric and diphasic T waves were observed in four and a broad QRS complex in two. Conduction times of only 0.10 occurred in three. Chronic alcoholism was probably the cause of the cardiac lesions in these patients. Whether vitamin B_1 or protein deficiency was the more important factor in causing the cardiac lesions could not be established.

Transfusion Reactions.—A survey was conducted at the St. Erik's Hospital in Stockholm into the incidence of reactions in conjunction with 6,899 transfusions by Olof Ramgren and co-workers (*Acta med. scandinav.* **162**:211, 1958). The incidence was 6%. No hemolytic reactions due to serologic incompatibility occurred. The rate for febrile reactions was 3.55%, allergic reactions 1.20%, and other reactions 1.20%. The use of disposable transfusion sets brought down the febrile reaction rate by 50%. The reaction rate increased with the number of previous transfusions. Rouleaux formation in the pretransfusion sample increased the risk of reaction. The age of the blood was of no consequence to the

reaction rate if administered within 14 days. If a patient had had a certain type of reaction after blood transfusion, an increased risk of reactions, and of the same type, might be expected on subsequent transfusions.

Thyrotoxic Myopathy and Polymyositis.—Four elderly women, two classified as having thyrotoxic myopathy and two as having polymyositis were described by Boström and Hed (*Acta med. scandinav.* **162**:225, 1958). The clinical findings presented great similarities in all four, and were initially misinterpreted as changes due to age. The following facts should be kept in mind for a differential diagnosis between these two forms of myopathy in the older age groups. Thyrotoxicosis often presents few symptoms in elderly patients, and can easily be overlooked; thyrotoxic myopathy is therefore likely to be confused with other forms of myopathy. The basal metabolic rate and urinary excretion of creatine often exhibit pathological values in both myopathies, and therefore have no value in differential diagnosis. In thyrotoxic myopathy, large doses of methylthiouracil produced a marked decrease in creatinuria or its disappearance within about 10 days, and even before any improvement in the muscular weakness had occurred. In polymyositis, this drug had no effect on creatinuria. In thyrotoxic myopathy, the histological changes in the muscle were generally slight, whereas severe damage to the muscle was observed in polymyositis. Progressive muscular weakness in elderly patients, particularly if it is combined with loss of weight, should not be ascribed to the process of aging without a thorough analysis, because certain forms of myopathy are amenable to effective specific or symptomatic therapy.

UNITED KINGDOM

Treatment of Cerebral Neoplasms by Cooling.—General hypothermia for the treatment of malignant growths has been tried but abandoned because prolonged hypothermia can cause cardiac fibrillation. Rowbotham and co-workers (*Lancet* **1**:12, 1959) devised a localized form of hypothermia for the treatment of cerebral neoplasms which they used on two patients with glioma and one with astrocytoma after tests had been made on excised human brains. Cooling was effected by a specially designed cannula, used in conjunction with a circulating pump, cooling coil, and circulating fluid reservoir. The cannula consisted of two concentric steel tubes, one for the delivery of cooling fluid and the other for its return to a reservoir. Before reaching the cannula the cooling fluid passed through a coil surrounded by a freezing mixture of solid carbon dioxide and acetone with a temperature of about –74 C. The temperature of the reservoir was kept at about –20 C. Tests on excised brains had shown that insertion of the cooling cannula enabled the temperature of the brain substance to be reduced locally to –20 C. The patients treated were beyond the aid of neurosurgery. Under general anesthesia the brain was exposed and the sterilized cannula inserted into the tumor. It was cooled to –20 C for 20 to 30 minutes. A core of solid frozen brain tissue 10 to 12 mm. in radius formed around the cannula, but brain tissue 2.0 to 2.5 cm. away from the cannula had a temperature of 30 C (86 F). The three patients recovered from the operation. It was shown that it is possible to freeze a local area of the brain without endangering life. One patient died later, another remained the same, and the mental condition of the third patient improved markedly.

Trials with Human Growth Hormone.—A panel appointed by the clinical endocrinology committee of the Medical Research Council investigated the action in man of growth hormone extracted from human pituitaries. Chemically this differs from ox growth hormone, which is inactive in man. Numerous pathologists throughout the United Kingdom cooperated by collecting human pituitaries from fresh cadavers. The acetone-dried glands were extracted with 0.3 M potassium chloride and repeatedly fractionated with alcohol and ammonium sulfate between pH 4.4 and 8.6. The final product was standardized against international standard ox growth hormone. From 10 to 30 mg. of the human growth hormone was given daily to two subjects without pituitary disease and to six with hypopituitarism. From two to eight days later increased nitrogen retention was observed, as shown by a fall in blood urea and urinary nitrogen levels. In addition there was retention of sodium, potassium, magnesium, phosphorus, and sometimes calcium. The amount of potassium, magnesium, and phosphate retained was only what would be anticipated for protein synthesis, calculated from the retention of nitrogen, but the amount of sodium was greatly in excess of this. A consistent rise in fasting blood sugar level was also observed.

Vitamin B_{12} Absorption.—By direct measurement of the distribution of radioactivity in the small intestine of patients given vitamin B_{12} labeled with cobalt-56, Booth and Mollin showed that the site of the absorption of the vitamin in man is the ileum (*Lancet* **1**:18, 1959). An oral dose of 1 mcg. of vitamin B_{12} was labeled with 5 μc of Co^{56}. The absorption was studied in patients undergoing laparotomy by examining the distribution of radioactivity in the small intestine three hours after the oral dose was given. An end-window Geiger-Müller counter covered with sterile rubber sheeting and a towel was used to measure the radioactivity. Starting from the duodenojejunal flexure the activity was measured at successive portions of the small intestine down to

the ileocecal valve. Absorption was maximum in the distal half or two-thirds of the ileum. This was confirmed by observations on vitamin B_{12} absorption in patients who had undergone resection or short-circuiting of the small intestine. Resection of the jejunum does not interfere with the absorption of the vitamin, but absorption is subnormal if more than about 7 ft. of ileum has been removed. This defect is not corrected by giving tetracyclines. Removal of the ileocecal valve does not interfere with the absorption of vitamin B_{12}. The authors suggested that the physiological absorption of vitamin B_{12} might, in man, be a definite function of the distal part of the small intestine which may contain a specific receptor mechanism for it. A congenital defect of the specific vitamin B_{12} receptor would explain the development of the pernicious anemia syndrome. The authors observed signs of vitamin B_{12} deficiency in patients who had undergone operations on the ileum. The onset of this deficiency was insidious and gradual. They considered that vitamin B_{12} should be given after all operations involving resection of the ileum.

Increase in Myopia.—Herbert Archer, an ophthalmologist of the Birmingham school health service, found more children in schools to be myopic than in previous years. He attributed this to the use and abuse of television. Unless people can be taught to ration the time spent viewing television myopia is likely to become commoner. Archer predicted that a large number of children would pass from the less serious types into the category of high myopia, which is the fourth largest cause of blindness.

Accuracy of Death Certificates.—A study on the accuracy of death certificates was included in the annual statistical review for 1957 (Statistical Review of England and Wales, Her Majesty's Stationery Office, 1958). Over a six-month period 10 large English hospitals arranged for a double death certificate to be issued for every patient dying in the hospital. One certificate was completed by a physician on clinical findings and the other by a pathologist after autopsy. The pathologists agreed with the physicians in 51% of cases, and to this were added another 28% in which the differences were technical rather than actual. Thus in about 80% of the deaths the cause as certified by the physician was confirmed by the pathologist. In 19% the latter found fresh evidence at autopsy that was denied the physician during life. This occurred mainly in the newborn and the aged. Cancer of the lung was underdiagnosed by the physicians, particularly in older patients. Of patients dying from this cause 30% were found to have unsuspected cancers at autopsy. It is evident that the death rate from cancer of the lung in Britain is even higher than it is reported to be. There was also disagreement between physicians and pathologists on the diagnosis of arteriosclerotic and coronary heart disease. They agreed on only 41% of cases, which corresponded closely to the 44% accuracy rate for myocardial infarction found by Paton at the Edinburgh Royal Infirmary. A number of cases mistaken for coronary disease by the physicians were in fact pulmonary embolism.

Carbon Monoxide Poisoning.—Recommendations made by the Medical Research Council (MRC) on the treatment of carbon monoxide poisoning have undergone revision. Three years ago the MRC issued a report stating that a carbon dioxide-oxygen mixture should not be used for the resuscitation of persons poisoned by carbon monoxide. The reason given at the time was that under the uncontrolled conditions of first-aid, carbon dioxide might accumulate to dangerous levels in the tissues. This argument was seriously challenged by experts in so far as carbon monoxide poisoning was concerned, on the grounds that the administration of an oxygen-carbon dioxide mixture increased the elimination of carbon monoxide and brought about a more rapid recovery. A special subcommittee was therefore set up by the MRC to consider the problem. As a result of experiments on animals and on human volunteers poisoned with carbon monoxide, it was concluded that the administration of a mixture of oxygen and carbon dioxide leads to a more rapid elimination of carbon monoxide from the blood than does oxygen alone. From this and clinical evidence the MRC subcommittee considers that on balance a mixture of 5% carbon dioxide in oxygen is more likely to facilitate recovery from carbon monoxide poisoning than oxygen alone, but that there is no advantage in increasing the amount of carbon dioxide beyond 5%.

Pleuropneumonia-like Organisms in Genital Infections.—Further evidence for the role of pleuropneumonia-like organisms (PPLO) in pathological conditions, particularly in nongonococcal urethritis (NGU) in men, was obtained by Klieneberger-Nobel (*Brit. M. J.* **1**:19, 1959). The identification of these organisms is difficult as they can be detected only by culture. Electron microscopy was abandoned as a means of identification, as the appearances could not be correlated with cultural methods. Urine specimens and discharge or scrapings from the urethra were obtained from men with NGU and related conditions, and from the vagina, cervix, or urethra of women from venereal, gynecologic, and prenatal clinics. Patients with Reiter's syndrome and a number of partners of patients from venereal disease clinics were also examined. The sediment from urine specimens was used for culture. PPLO were found to be absent from the urine of 97% of healthy men examined. One had NGU and another was a symptomless carrier of the organisms. PPLO were completely absent from the urine of 43

prepuberal boys seen in the medical wards of a hospital. The discharges and scrapings from men from the venereal disease clinics were positive for PPLO in 25% of 201 patients. The highest number of positive results (48%) was obtained in those that had recently acquired NGU; 30% of the men with gonorrhea harbored PPLO. The organisms were present in the scrapings of 10% of the patients with Reiter's syndrome.

The incidence of PPLO was found to be much higher in the women patients; 56% of those attending venereal disease clinics were infected. In those with gonorrhea, whether treated with penicillin or not, nearly 90% carried the organisms in the urethra, vagina, or cervix. Surprisingly enough 23.5% of the pregnant women examined harbored PPLO in the cervix. The incidence in gynecologic patients of a London hospital was 17%. PPLO were not found in the synovial fluid of patients with Reiter's syndrome, and only rarely in the urethral discharge. This refutes the commonly held view that Reiter's syndrome and NGU have a common cause. The author's observations show that genital strains of PPLO are absent before puberty, and rare in healthy young men and women. They are associated with recently acquired urethritis in a high proportion of men suffering from NGU, and with cervicitis, vaginitis, and urethritis in women. They are often present in patients with gonococcic and trichomonal infections and are particularly likely to be transferred by sexual intercourse.

Spirochetal Rat Bite Fever.—Rat bite fever caused by infection with Spirillum minus is extremely rare in England, no case having been reported for over 30 years. Edmunds and Tilley described a case occurring in Edinburgh due to a mouse bite (*Lancet* **2**:1211, 1958). No reference to mice as a source of infection in this country has been reported before. An 11-year-old boy was bitten by a mouse and one week later developed a severe headache and pyrexia. Two weeks after the bite the puncture marks were painful, swollen, and red, and large spots appeared on the backs of his arms and legs. The pyrexia persisted, with intermittent fever around 103 F. The conjunctivas were injected, the eyelids were swollen, and the patient had an intractable headache. Appetite and weight loss occurred and a moderate soft enlargement of the principal lymph nodes was noted. The presence of Sp. minus was demonstrated by inoculation of mice and guinea pigs with the boy's blood. Large doses of penicillin were given. Although there is a widespread belief that mice are harmless, the risk to those handling them in the laboratory and during disinfestation should be more generally known.

Oral Treatment of Ringworm.—It was shown by Gentles that guinea pigs experimentally infected with Microsporon canis and Trichophyton mentagrophytes quickly responded to small oral doses of the antibiotic griseofulvin, which was isolated from Penicillium griseofulvum (*Nature* **182**:476, 1958). The antibiotic is evidently absorbed and secreted into the dermis, as it was found by Gentles in the hair of treated animals. Williams and co-workers gave the antibiotic in oral doses of 0.5 Gm. four times a day to nine patients with clinical Trichophyton rubrum infection of the skin or nails and one with Microsporon audouini infection of the scalp (*Lancet* **2**:1212, 1958). No local treatment was given. The antibiotic caused rapid relief of itching, growth of infected nails, loss of hyperkeratosis, and disappearance of the fungus from nail scrapings. In the one patient with ringworm of the scalp, the hair did not fluoresce under Wood's light three weeks after beginning treatment. The toxicity of griseofulvin is low and no side-effects were observed. These preliminary results support the hope that griseofulvin may be of use in the oral treatment of ringworm.

Surplus Women Declining.—For many years there have been more women than men in Britain. If the present trend continues and there are no more wars there will soon be as many men as women, according to the Registrar General's report, which states that the long-continued increase in the ratio of women to men, which started in 1821, or earlier, has now ended. In the last century, although from 40 to 50 more boys were born for every 1,000 girls, there was an excess of females over males because of the higher death rates for boys. About 60 more boys are now born for every 1,000 girls, but the death rate of boys is falling. At the last census women were still in the majority—1,082 to every 1,000 men. The report states that divorced women outnumber divorced men 130,000 to 79,000, because more men than women marry again. There are 2,319,000 widows, but only 739,000 widowers. This is attributed to the fact that women, particularly married women, live longer than men.

Antibiotics and the Common Cold.—In a letter to the *Lancet* Professor Garrod deprecates the use of chloramphenicol and other antibiotics, which have recently been recommended for the prevention of complications, in the treatment of the common cold. His chief reason for proscribing chloramphenicol is because it is known to cause bone marrow damage, and therefore its use is unjustified for trivial purposes. If an antibiotic must be used for the treatment of colds it should be penicillin, which is cheaper, safer, and can be used in the form of a spray, snuff, or pastille, but Garrod objects even to this form of treatment as it may lead to sensitization. If all common colds were generally treated by antibiotics it would add $315,000,000 to the annual drug bill of the nation.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Periarteritis Nodosa: Review. P. Bro-Rasmussen. Ugesk. laeger **120**:1481-1489 (Nov. 6) 1958 (In Danish) [Copenhagen].

During the last 10 years 17 patients with periarteritis nodosa were admitted in the Rigshospitalet in Copenhagen. Of the 9 patients in whom diagnosis was made during life, 7 are living from 6 months to 9 years after the diagnosis. Periarteritis nodosa is counted among the collagen diseases, which also include chronic polyarthritis, lupus erythematosus disseminatus, thrombotic thrombocytopenic purpura, scleroderma, polymyositis, and dermatomyositis. Morphologically, all are characterized by marked changes in the connective tissue. Periarteritis nodosa occurs most frequently between the ages of 20 and 40 years and is seen more often in men than in women. The picture is polymorphic. Long-continued fluctuating fever is the main symptom. The frequency of admissions and the number of diagnoses made in life support the concept that the disease is increasing in frequency. Periarteritis nodosa should be considered in unusual combination of symptoms and in vague progressive cases, with fever, muscular asthenia, and loss of weight. The diagnosis is supported by information on allergic manifestations, hypersedimentation, hypergammaglobulinemia, transient electrocardiographic changes, and transient roentgenologic pulmonary changes. Only skin and muscle biopsies afford certain diagnosis. The treatment consists of the administration of 11-oxysteroids and is otherwise symptomatic. The prognosis is unfavorable. There seems, however, to be a tendency to remission in most cases in which the viscera are not involved. The disease may have an acute course with fatal outcome; the course may also be insidious and protracted or show remissions and acerbations with increasing symptoms of ischemic lesions of the different organs.

The place of publication of the periodicals appears in brackets preceding each abstract.

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Negative L. E.-Cell Phenomenon in True Systemic Lupus Erythematosus. P. Formijne and F. van Soeren. Lancet **2**:1206-1207 (Dec. 6) 1958 [London].

The authors report on a 53-year-old man with the typical aspect of systemic lupus erythematosus, in whom the L. E.-cell test gave completely negative results. Further immunological investigation showed that the Wassermann test could not be carried out, owing to anticomplementary activity of the patient's serum. It was then considered that a connection might exist between this activity and the negative L. E.-cell phenomenon. When excess normal fresh human complement was added to the patient's serum, the L. E.-cell phenomenon became clearly positive. Positive L. E. serum was heated at 56 C (132.8 F) for between 30 and 60 minutes. Fresh leukocytes washed in sodium chloride solution and fresh leukocyte nuclei washed in sodium chloride solution gave negative results with this inactivated serum concerning the L. E.-cell phenomenon; after addition of fresh human or guinea pig serum, a few rosettes and a few classic L. E. cells were found. The patient's condition deteriorated, and he died in cardiac failure. The diagnosis of systemic lupus erythematosus was confirmed by autopsy.

Free-acting complement plays an important role in the production of the L. E.-cell phenomenon. Inactivation of a positive L. E. serum by heating is possible, when it is used with washed leukocytes and washed leukocyte nuclei. After addition of human or guinea pig complement to this system, a weakly positive L. E.-cell phenomenon reappears. The L. E.-cell phenomenon can be negative, notwithstanding the presence in the serum of the specific L. E. factor and of complement, if complement-inhibiting substances are also present. In this case the L. E.-cell phenomenon can be demonstrated by the addition of fresh complement. The L. E.-cell phenomenon may perhaps be inhibited by lack of complement.

Metastasizing Carcinoid. L. Heilmeyer and R. Clotten. German M. Month. **3**:338-340 (Nov.) 1958 (In English) [Stuttgart, Germany].

The authors report on a 56-year-old man with metastasizing carcinoid of the small intestine, whose case was peculiar with regard to its clinical aspects and metabolic behavior. The clinical course of the disease was more severely malignant than usual, with a greatly enlarged liver, the surface of which

showed numerous nodules varying from the size of a pea to that of an apple. There were bouts of high fever, and the erythrocyte sedimentation rate was considerably increased. Flushes occurred very frequently and were particularly severe. Oliguria and tachycardia were present in the absence of fever. In contrast to these findings, the intermittently normal excretion of hydroxyindolacetic acid and the increased excretion of tryptophan in the urine were surprising and difficult to interpret. Another substance which gave the same color reactions as hydroxyindolacetic acid also was observed; it might have been hydroxyindolacetaldehyde, another intermediate-stage decomposition product during the oxidation of 5-hydroxytryptamine to hydroxyindolacetic acid, or the gluconate of this acid. Other tryptophan derivatives were present in the electrophoretic pattern of the urine. A particularly severe flush was observed after 2 intravenous injections, each containing 50 mg. of 5-hydroxyindolacetic acid; the excretion of hydroxyindolacetic acid in the urine was simultaneously increased, and 38.3 and 35.1 mg. of the administered amounts was recovered from the urine within 24 hours. A severe flush also was observed after the intramuscular administration of 2.5 mg. of reserpine.

A possible explanation for the puzzling normal excretion of 5-hydroxyindolacetic acid and the increased tryptophan excretion is suggested as follows. A loss of the enzymes, which contribute to the oxidative transformation of 5-hydroxytryptamine into 5-hydroxyindolacetic acid, may result from the dedifferentiation of the carcinoid cells; 5-hydroxytryptamine may then accumulate in the cells, and finally a retransformation in tryptophan and hydroxytryptophan, respectively, may occur, which cannot be distinguished with the techniques used. Though not verified, this concept seems plausible. Another explanation would be that the clinical manifestations in this patient were not elicited by hydroxytryptamine but by another tryptophan derivative. Clinically the conclusion is inescapable that extensive carcinoid metastases may be associated with a normal excretion of hydroxyindolacetic acid in the urine. In such cases simultaneous determination of tryptophan excretion may be of diagnostic value.

Diagnostic Value of Needle Biopsy of the Liver. A. Lattanzi and U. Urbano. Omnia med. **36**:185-209 (May-Aug.) 1958 (In Italian) [Pisa, Italy].

Specimens of the liver were obtained by needle biopsy from 53 hospitalized patients. Primary or secondary neoplastic disease was present in 17 patients, subacute or chronic hepatitis with progression toward sclerosis in 17, cirrhosis of the liver in 14, systemic blood disease in 2, and reticuloendotheliosis in 1. Needle biopsy of the liver was the main diagnostic procedure in 21 patients; it contributed to the formulation of the diagnosis in 25; it had insignificant diagnostic value in 5; and it gave an erroneous response in 2. Of the 14 patients with cirrhosis of the liver, needle biopsy of the liver established the diagnosis in 5 patients; it confirmed a previously established diagnosis by clinical means and laboratory findings in 8; and it gave disagreement with the clinical picture in 1 [It seems that the specimen of the last patient was obtained from the intact part of the liver.] Needle biopsy of the liver is particularly useful for an early diagnosis in cirrhosis of the liver.

Of the patients with subacute or chronic liver disease, needle biopsy of the liver was the main diagnostic means in 7 patients; it confirmed a previously established diagnosis in 7; and it was of insignificant diagnostic value in 2. Needle biopsy of the liver in subacute or chronic liver disease may also have a prognostic value; it can aid in detecting a latent sclerotic progression at a stage when the disease appears to be clinically cured. Of the 17 patients with primary or secondary neoplastic disease, needle biopsy of the liver was the main diagnostic means in 10 patients; it confirmed a previously established diagnosis in 4; it was of insignificant diagnostic value in 2; and it gave a discordant response with other procedures in 1. Needle biopsy of the liver in patients with neoplastic disease was supported and guided by the findings of laparotomy. The authors conclude that needle biopsy is an innocuous and fairly reliable diagnostic procedure for the establishment of the histological picture of various hepatic diseases and that it seems to be superior to other laboratory methods.

The Role of Hemodialysis (Artificial Kidney) in Acute Poisoning. G. E. Schreiner. A. M. A. Arch. Int. Med. **102**:896-913 (Dec.) 1958 [Chicago].

The role of the artificial kidney in human poisoning may be considered from 2 points of view: the removal of (1) dialyzable poisons and (2) nephrotoxic poisons; the latter produce damage to the kidneys and are not different from other causes of acute renal insufficiency. In some instances, general toxicity may be produced from the poison itself, while in others it is a produce of the uremic syndrome. The effective use of hemodialysis is based on the following assumptions: 1. The poison molecule can diffuse through cellophane from plasma water and has a reasonable removal rate, or dialysance. 2. The poison is distributed in accessible body-fluid compartments. If substantial fractions of the absorbed poison dosage are bound to protein molecules, concentrated in important fluid compartments (e. g., cerebrospinal fluid), or attain a significant intracellular concentration, then effective dialysis will be sharply limited. This restriction is diminished, however, if the "loculated" portion is

in diffusion or chemical equilibrium with a significant moiety in the plasma water. 3. There is a relationship between toxicity and the blood concentration and duration of the body's exposure to this circulating poison. 4. The amount of poison dialyzed constitutes a significant addition to the normal body mechanisms for dealing with the particular poison.

Many types of acute poisons are not susceptible to hemodialysis when measured against these considerations. Anticholinesterase compounds, as an extreme example, act much too rapidly for a favorable relationship between blood level and clinical toxicity. The same is probably true of the tissue necrosis due to the phosphorus content of rat-paste and matchstick poisoning.

The author is concerned with poisons for which removal by dialysis has been demonstrated by chemical measurement or reversal of clinical state. These include various barbiturates and salicylates, bromide, thiocyanate, ammonia, strontium, radiocalcium (Ca^{45}), tritium, and glutethimide. The author reviews the role of hemodialysis in the study and treatment of acute poisoning on the basis of 8 years' experience embracing 24 patients with dialyzable poisons and 15 patients with nephrotoxic injury. Survival rates were 83 and 47%. Barbiturate, salicylate, bromide, glutethimide (Doriden), and diphenylhydantoin (Dilantin) poisoning are reviewed in detail, with illustrative case histories appended. The first known instance of successful dialysis of severe methyl salicylate poisoning is presented, with reduction in blood salicylate level from 110 to 29 mg. per 100 cc. Early dialysis is suggested to abort the full clinical picture from dialyzable poisons and nephrotoxic injury.

Treatment of Chronic Asthma with Prednisolone: Significance of Eosinophils in the Sputum. H. M. Brown. Lancet **2**:1245-1247 (Dec. 13) 1958 [London].

The subcommittee on clinical trials in asthma of the British Medical Research Council in 1956 had found no real advantage in cortisone acetate treatment of chronic asthma, compared with bronchodilator drugs. Analysis suggested that its methods were not beyond criticism; so general practitioners in the Derby area were asked to refer chronic asthmatic patients to the chest clinic to take part in another trial with prednisolone. This included patients who were already receiving steroid therapy, as well as those who joined the trial later. There were 90 patients in all. The trial was limited to patients who had had chronic bronchospasm for at least a year, and who had proved refractory to all other forms of treatment over at least one month. Early in the trial it was found that the distinction between asthma and chronic bronchitis with predominant bronchospasm was difficult.

The discovery of eosinophilic sputum in patients who responded dramatically to prednisolone prompted the improvisation of a method of examining the sputum and made it possible to separate the true asthmatics with eosinophilic sputum from the others. The success of this method suggested the examination of the sputum of patients receiving prednisolone. Corticosteroids clear the blood of eosinophils, but it was found that this did not happen in the sputum. Eosinophils in large numbers in the sputum were associated with a good response to prednisolone, and few or no eosinophils with a poor response.

Except when bronchospasm was very severe, the dose given was 5 mg. thrice daily for a week, followed by reassessment and adjustment of dose. All patients were given notes warning them of the dangers involved in prednisolone therapy. As a further safeguard, notes on the dangers of treatment were issued to family physicians. Each patient was told to take as little prednisolone as possible to keep him from wheezing. When wheezing had ceased for a few days, the dose was reduced by 2.5 mg. every 3 days until wheezing returned slightly. It should then be increased by 2.5 mg., so that wheezing disappeared again, and then continued at that level for about 10 days, when a further attempt should be made to reduce the dose. Thus, the patient was constantly trying to reduce the dose and finally stop treatment. Often patients were too enthusiastic in reducing dosage, so that spasm got out of hand and 15 mg. a day was needed for a week or so to control it. With these methods and by careful supervision and the use of antibiotics when needed, the risk of side-effects and complications was minimized. The screening technique for eosinophils in the sputum is described.

In some patients treatment with prednisolone had to be continued for a long time. Which is the lesser evil, disabling asthma or the dangers of long-term prednisolone treatment? All patients who had to make this choice chose to continue treatment. The elderly bronchitic patient with severe bronchospasm rarely benefited. Younger patients who obtained complete relief from bronchospasm usually had little or no residual dyspnea once the bronchospasm had disappeared. On the other hand, older asthmatics in whom emphysema had developed were still dyspneic. Experience showed that, if there was no improvement within 2 weeks on 15 or 20 mg. of prednisolone per day in the absence of purulent sputum, no significant benefit would be derived from continuing treatment. Prednisolone was used in children only when antispasmodics were of no avail, when there was emphysema and a poor prognosis, when the child had constant bronchospasm punctuated by exacerbations, and after eosinophils had been demonstrated in the sputum. Though prednisolone is effective in suit-

able cases, it never does more than suppress the asthmatic state, and it does not abolish eosinophils in the sputum, though the quantity is much reduced.

Value of Thyrotropin Stimulation Test in Diagnosis of Myxedema. T. Friis, L. K. Christensen and M. S. Andersen. Ugesk. laeger **120**:1545-1548 (Nov. 20) 1958 (In Danish) [Copenhagen].

Investigations confirm that thyrogenic myxedema in patients given thyroidin preparations can be excluded if the patients react to thyroid-stimulating hormone (TSH) with fairly normal absorption of radioiodine (I^{131}) in the thyroid gland. TSH tests with 4 U.S.P. units of TSH were carried out in 33 patients treated with thyroidin. Eleven had thyrogenic myxedema; they did not react to TSH with increased absorption of I^{131}. Of the 22 patients who presumably did not have myxedema at the start of treatment, 6 did not react to TSH; the thyroid gland is thought to have undergone atrophy in these cases as a result of thyroidin treatment.

Ammonia Intoxication Treated by Hemodialysis. J. E. Kiley, J. C. Pender, H. F. Welch and C. S. Welch. New England J. Med. **259**:1156-1161 (Dec. 11) 1958 [Boston].

Increased concentration of ammonia has been observed in many patients with hepatic coma. On the basis of investigations to determine whether ammonia present in the blood could be removed by a Kolff type of artificial kidney, the authors reported in 1955 that ammonia was removed by an artificial kidney with a dialysance varying from 50 to 80 ml. per minute when blood flow was 100 ml. per minute and membrane area was 12,000 sq. cm. They now report the application of hemodialysis to 5 patients who were comatose with ammonia intoxication. All these patients had advanced liver disease and lapsed into coma, with elevated blood ammonia levels, after massive gastrointestinal hemorrhage. All had ascites, and the prognosis was considered sufficiently poor to warrant trial of a new treatment. All were treated by esophageal tamponade, gastric lavage, and catharsis. A modified Kolff rotating-drum type of artificial kidney was used.

Three patients were treated by dialysis in the hope of relieving overwhelming ammonia intoxication of the exogenous type. No untoward effect of dialysis was observed. The first 2 patients came out of coma after the dialysis. Dialysis in the third patient was too limited by ordinary standards (only 11 liters of blood ran through the artificial kidney) to be of much therapeutic significance. This patient did not regain consciousness and died 2 days after the dialysis was terminated at a time when the first 2 patients were again alert and rational. In these 3 patients ammonia intoxication was not associated with any other biochemical disorder of comparable significance. In the other 2 patients severe ammonia intoxication was associated with other biochemical abnormalities. In each of these last 2 patients dialysis removed large amounts of ammonia nitrogen and other nonprotein-nitrogen constituents of the blood. In one of these 2 patients the temporary improvement noted was dramatic. Thus, 4 of 5 patients showed clinical improvement after effective dialysis. In the patient who died, dialysis was ineffective because of blood clotting. The authors conclude that ammonia may be removed by hemodialysis from patients suffering from ammonia intoxication, and that removal of ammonia by dialysis may be beneficial.

Microlithiasis of Pulmonary Alveoli. D. Hojman, R. B. Podio and O. C. Barreiro. Rev. Asoc. méd. argent. **72**:411-417 (Oct.) 1958 (In Spanish) [Buenos Aires].

Microlithiasis of the pulmonary alveoli is a rare familial and congenital disease of unknown origin. The disease consists of absorption of calcium salts by the lung parenchyma and the formation of microliths of various sizes, which occupy the pulmonary alveoli in innumerable quantities. The disease follows its course without symptoms or in presence of mild dyspnea for several years. It causes chronic cor pulmonale and insufficiency of the heart. It can be detected by chance during a routine roentgenologic examination of the chest. The roentgenograms of the chest are characteristic, showing complete bilateral opacification of the lungs, which involves the whole structure with the exception of the apex. The respiratory symptoms reported by the patients, as well as those heard on auscultation of the chest, are out of proportion to the extensive lesions of the lungs, as shown in the roentgenograms. Of the total 44 cases reported in the literature, an autopsy was performed in 12 cases, and a biopsy in 11. The pulmonary disease is restricted to the pulmonary parenchyma, the pulmonary alveoli, and the consequent pulmonary heart. All other organs and structures are normal. The microliths are free within the alveoli, the walls of which are normal and in rare cases involved by fibrosis. On touch, the lung gives the sensation of being a pumice stone. Blood vessels, bronchi, and pleura of the involved lungs are normal. If the lung tissue is put in water, it sinks. On cutting, it cracks like cutting metal. The cutting surface looks as if it were sandpaper.

A man, 58 years old, reported for consultation with symptoms of insufficiency of the heart. He had had moderate dyspnea for 18 or 20 years. Clinical examination showed a chronic pulmonary heart and very mild respiratory disorders detected on auscultation of the chest. The roentgenograms of the chest were typical of microlithiasis of the pulmonary alveoli. All other organs and structures were normal. It was learned that 2 brothers of the pa-

tient had died of the same disease and that his 5-year-old son apparently had the same disease in an early stage. Prior to death the patient was given a diagnosis of microlithiasis of the pulmonary alveoli. Partial autopsy with histological studies of tissues from the lower lobe of a lung confirmed the clinical diagnosis.

Mild and Severe Varieties of Erythema Multiforme Exudativum: Observation of Several Cases. G. Manganelli. Gior. clin. med. **39**:1327-1353 (Sept.) 1958 (In Italian) [Bologna, Italy].

The author reports on 15 patients with erythema multiforme exudativum, 7 of whom had the mild variety, 4 the severe variety, and 4 the intermediate variety of the disease. In addition to the conventional symptoms, the patients with the mild variety developed high fever. The patients with the severe variety, also known as the Stevens-Johnson syndrome, manifested some, but not all, of the common features of this syndrome, which ran a fatal course in 2 patients. The intermediate variety was characterized by mild symptoms with involvement of the gastrointestinal tract in all 4 patients and an affection of the kidneys in 3. The renal lesions appeared during the resolutive phase of the disease and persisted for a certain period of time after diarrhea, vomiting, and cutaneous lesions had subsided.

The author concludes that in this series the mild and the severe varieties of erythema multiforme exudativum appeared to be facets of the same disease, because some of the symptoms which were not apparent in one were present in the other. Involvement of the viscera developed in both varities, and a higher erythrocyte sedimentation rate was observed in both. The Stevens-Johnson syndrome seemed to represent only one form of erythema multiforme exudativum. The clinical features of erythema multiforme exudativum in some of these patients were similar to those of the collagen diseases. Among these were a precarious state of health, arthralgic pain, and cutaneous erythema.

The Incidence of Peptic Ulceration in Some African Tribal Groups. A. B. Raper. Tr. Roy. Soc. Trop. Med. & Hyg. **52**:535-546 (Nov.) 1958 [London].

The incidence of gastric and duodenal ulcer in 3 groups of people of diverse origins, living in the neighborhood of Kampala, Uganda, was assessed by means of a consecutive series of postmortem examinations. For male subjects, the gross incidence of peptic ulcer in the local people was 13.68%, in Nilotic immigrants 5.4%, and in immigrants from the southwest (especially Ruanda) 20.6%. The generally high incidence, 15.3% in men and 4.65% in women, is in contradiction of previous reports from tropical Africa. It is suggested that the causes of peptic ulcer are abundantly operative in tropical Africa but that the conditions in which the disease may be brought to notice are rarely fulfilled.

The results of this survey give confirmation to the view that peptic ulcer is commoner in immigrants from the southwest than in the people of central Uganda, but it was an unexpected finding that another group of immigrants, the Nilotics, should show a lower incidence than the local people. The author feels that it is not necessary to postulate variations in "racial" susceptibility to ulcer, at least as the immediate cause, for in the population from which these data are drawn the 3 groups are exposed to very different conditions of life. The immigrants from the southwest represent the section of the community subject to the greatest stress; their life is the hardest, their food the poorest, often long intervals elapse between their meals, the prevalence of disease is greatest among them, and fears for the future must be constantly present in their minds. These considerations offer an entirely adequate explanation for any proneness to ulcer that they may exhibit. They certainly offer a marked contrast to the Nilotic immigrants, in whom the lower incidence of ulcer could well be related to the fact that these people are better fed and have a more carefree attitude toward life, a consequence partly of their greater efficiency as wage earners. The local people occupy in these respects a position intermediate between the 2 immigrant groups. Thus, if any influence is to be attached to innate susceptibility to ulcer, it depends in these 3 groups on the success with which they face the complexities of life, and thereby encourage or impede the action of the well-recognized etiological agents of peptic ulcer.

Intestinal Polyposis and Mucocutaneous Pigmentation (Peutz-Jeghers Syndrome): Further Comments and Report of an Additional Case. L. C. Bartholomew and D. C. Dahlin. Minnesota Med. **41**:848-852 (Dec.) 1958 [St. Paul].

The authors point out that an earlier report from the Mayo Clinic on intestinal polyposis and mucocutaneous pigmentation (Peutz-Jeghers syndrome) described 6 new cases and reviewed 69 cases reported in the literature to the end of 1955. Since then a sufficient number of additional cases have been presented to justify further reflections on this disease, particularly on the potentially malignant character of the polyps. The authors present the history of an 82-year-old man, who in addition to urinary retention had experienced a severe substernal pain, and in whom an electrocardiogram showed the typical findings of an acute anteroseptal myocardial infarction. The patient died 6 hours later. Postmortem examination revealed coronary sclerosis, a recent infarct in the apex and anterior wall of the left ventricle with rupture of the myocardium into the pericardium, benign prostatic hypertrophy, and bilateral

hydronephrosis. An incidental finding was that of single polyp, 1 cm. in diameter, in the fundus of the stomach and 6 polyps in the colon. The examiner's awareness of the aspects of the Peutz-Jeghers syndrome led to a search for, and the demonstration of, the characteristic pigment on the mucosa of the lips. Microscopically, all the polyps were benign.

In the 2 years that have elapsed since the earlier review of 75 cases, 42 additional cases of this syndrome came to the authors' attention, bringing the total to 117. The pigment was present on the lips in 115 of the 117 patients, thus making this the single most important physical sign. It was noted on the buccal mucosa in 103 of the 117 patients. The polyps were present in some part of the small intestine in 108 of the 117 patients. The exceptions included 7 patients with polyps in the rectum alone, 1 with polyps in the colon and stomach, and 1 with polyps in the rectum, colon, and stomach. Episodes of abdominal pain and some form of gastrointestinal bleeding were the major symptoms. Recurrent attacks of colicky abdominal pain occurred in 99 of the 117 patients. About 55% of the patients have some evidence of the familial nature of this disease.

The major aspect of this syndrome that remains debatable pertains to the potential malignant nature of the polyps. The peculiar histological characteristics of the polyps that the authors were able to study led to the suggestion that these tissue excrescences represent a developmental abnomality rather than true adenomatous polyps. The 3 predominant types of cells of the normal mucosa of the small intestine, namely, columnar absorbing cells, goblet cells, and coarsely granular Paneth cells, were found within the jejunal and ileal polyps that were studied in 5 patients. The authors feel that the over-all pattern of these polyps strongly suggests that they are the result of a growth disturbance similar to that which produces hamartomas of the lungs. None of the polyps which they studied in the Peutz-Jeghers syndrome appeared malignant or even premalignant. However, although the colonic and rectal polyps studied in patients with the Peutz-Jeghers syndrome have appeared benign, there is no evidence to suggest that these patients are immune to the development of ordinary adenomatous polyps and carcinomas in these locations.

Intolerance for Gluten in a Patient with Regional Ileitis. J. R. Chan Jon Chu. Nederl. tijdschr. geneesk. **102**:2150-2154 (Nov. 1) 1958 (In Dutch) [Amsterdam].

The author presents the history of a 26-year-old woman who for nearly a year had been troubled with abdominal pains and constipation. After a more severe attack of pain accompanied by vomiting, diarrhea developed, which persisted. There were 3 or 4 loose or watery stools daily. Loss of weight resulted. "Chronic appendicitis" and later tuberculous peritonitis were suggested. Diarrhea and weight loss continued despite conservative treatment. Regional ileitis was diagnosed at laparotomy, and an ileocecal resection was performed. Twenty months later, at a second operation for regional ileitis, the lower third of the remaining small intestine was resected. Abdominal pains, diarrhea, and loss of weight recurred after both operations, and after the second operation the diarrhea gradually became more severe, and symptoms of malabsorption developed. Fat balance studies revealed extreme steatorrhea. The patient was treated with a gluten-free diet; prompt improvement followed, and the fat absorption rose. The gluten-free diet combined with up to 25 mg. of prednisone daily effected no increase in fat absorption. Treatment with gluten-free diet alone resulted in complete clinical recovery.

Angiographic, Functional and Clinical Aspects of Obliterating Arteriopathy of the Lower Extremity and Their Relationship. V. Uberti and G. Japichino. Omnia med. **36**:130-183 (May-Aug.) 1958 (In Italian) [Pisa, Italy].

The authors investigated the correlation between morphologic, functional, and clinical aspects of occlusion at various sites of an affected artery in 487 patients with arterial occlusion of the lower extremity. Obstruction of the superficial femoral artery was present in 112 patients (22.4%); it was related to atherosclerosis in 106 patients and to thromboangiosis in 6. Peripheral blood flow was in most instances fairly adequate in relation to the collateral circulation. Intermittent claudication developed in 104 instances, pain at rest in 17, cyanosis in 14, and ulcer in 4. Occlusion of the popliteal artery was present in 19 patients (3.8%); it was related to atherosclerosis in 11 patients and to thromboangiosis in 8. Digital plethysmography revealed that peripheral blood flow was more pronounced in patients with occlusion of the popliteal artery than in those with occlusion of the superficial femoral artery. Clinical symptoms were also more marked; intermittent claudication affected all patients; trophic lesions and pain at rest were also more intense.

Occlusion of the femoral–popliteal tract developed in 23 patients. The occlusion was severe, and plethysmograms showed considerable reduction in peripheral blood flow. Severe clinical symptoms were directly related to the reduced peripheral blood flow. Occlusion of the anterior tibial artery was present in 21 patients. Plethysmograms showed variations from extreme reduction to almost normal pattern in peripheral blood flow. Many instances of severe ischemia were observed: pain at rest in 12 patients, hypothermia in 10, and cyanosis in 12. Occlusion of the posterior tibial artery was present in 27 patients. Total occlusion was more frequent than partial occlusion. Plethysmographic patterns

showed a considerable decrease in peripheral blood flow at rest and a marked increase after reflex vasodilation. Multiple occlusions of the arteries of the leg, which were mostly related to thromboangiosis, were observed in 116 patients (23.2%). Plethysmograms showed a considerable decrease in peripheral blood flow. The main clinical feature was a rapid development of ischemia. Associated occlusions of the arteries of the thigh and the leg were present in 67 patients. Reduction in peripheral blood flow was considerable and was often very high. Intermittent claudication, pain at rest, and necrotic lesions were frequent and severe.

The clinical symptoms related to arterial occlusion in patients of this series were often worse than those usually observed at corresponding sites of obliterated arteries of the lower extremity. The succession of clinical symptoms reflected the gradual development and the extent of arterial lesions.

Kahler's Disease and Proteinuria. J. Warter, P. Métais and J.-M. Mantz. Semaine hôp. Paris 34:2919-2930 (Dec. 4) 1958 (In French) [Paris].

The authors studied the incidence of proteinuria in 16 patients with multiple myeloma (Kahler's disease). Renal manifestations generally appeared simultaneously with pathological changes in the bones, but in one patient the occurrence of anuria led to the diagnosis of multiple myeloma. Proteinuria was manifested in one patient several months and in another patient 4 years before other symptoms and signs of multiple myeloma appeared. The filter-paper electrophoresis of urine from patients with proteinuria revealed more often a mobility of gamma globulins, and more rarely of beta globulins, with or without a corresponding serum globulin peak. Thus, in 3 of the 16 patients globulinuria was the initial symptom and the premonitory sign revealing multiple myeloma. The diagnostic value and prognostic significance of electrophoretic analysis of urine are emphasized, particularly in patients with severe proteinuria of unknown origin.

The various physicochemical aspects of Bence Jones proteins are considered, such as their thermal solubility, their electrophoretic pattern, and their amino acid composition. The problems regarding the origin of Bence Jones proteins, their release into the circulation, and their rapid excretion through the kidneys due to their low molecular weight (about 44.000) are discussed. Nitrogen metabolism was studied in patients with multiple myeloma by evaluating the intestinal absorption of methionine and of glycine labeled with radio carbon (C^{14}). The intensity of protein synthesis, which characterizes myeloma, entails an indubitable state of nitrogen deficiency. The hyperabsorption of the amino acid administered in such cases seems to be a manifestation of this deficiency.

The Clinical Significance of Diverticulosis. R. S. Boles Jr. and S. M. Jordan. Gastroenterology 35:579-582 (Dec.) 1958 [Baltimore].

The authors report on 134 men and 160 women with diverticulosis, who were studied at the Lahey Clinic in Boston. The average age of the patients was 55 years. One hundred nineteen patients (40%) had a history of definite laxative abuse, and 33 patients (11%) complained chiefly of diarrhea. The medical management of the patients with diverticulosis was the same as that of those with irritable colon, namely, a regimen of diet, medication, and hygiene designed to combat spasm, since it has long been the opinion of one of the authors that spasm at the mouth of the diverticulum causes retention of material within the diverticulum with resultant inflammation and infection. During the average follow-up period of 15 years with an undetermined and undoubtedly varying degree of fidelity to the prescribed treatment, complications were noted in 119 of the 294 patients, with the following distribution: diverticulitis in 73 patients (24.8%); hemorrhage in 16 (5.4%); obstruction in 15 (5.1%); and perforation or fistula in 15 (5.1%). Of the 73 patients with diverticulitis, 28 (38%) had superimposed complications, and of the 221 patients with only diverticulosis, 18 (8.1%) had complications without evidence or history of clinical diverticulitis; thus, nearly 5 times as many patients with active diverticulitis had superimposed complications as did those with diverticulosis. Forty patients, i.e., more than half of the 73 with diverticulitis, had only one attack of this complication. Multiple attacks of diverticulitis in the other 33 patients were associated with more than twice as many complications (57.5%) as were single attacks (22.5%). Cancer occurred in 16 (5.4%) of the total group of 294 patients with diverticulosis, with no increase of incidence in areas of diverticulosis or diverticulitis.

These findings have special significance at this time when surgical advances have produced much greater safety in the single-stage resection for diverticulitis and a resultant enthusiasm among many surgeons for earlier radical treatment of this disease. According to the authors, diverticulitis should still be regarded as a medical disease until complications make surgical treatment necessary.

Old and New Tests for Bilirubin in the Urine. J. M. Bleyer and F. Steigmann. Am. J. Digest. Dis. 3:947-952 (Dec.) 1958 [New York].

The investigations described here were undertaken to compare the efficiency and usefulness of 2 older (Rosenbach and Smith) and 2 newer (Franklin and Ictotest) tests for the detection of bile in the urine. Two hundred forty-seven freshly voided morning urine specimens of 129 patients with icteric scleras and clinical and biochemical (liver profile)

signs of liver disease were examined for bile and albumin; simultaneously blood was drawn for the determination of the serum bilirubin (van den Bergh). Each urine sample was tested for albumin with 20% sulfosalicylic acid and for bile with each of the following tests: 1. Rosenbach's modification of the Gmelin test: The urine is filtered through a small filter paper. One drop of yellow nitric acid is introduced into the cone of the paper. The appearance of any colored ring indicates positivity. 2. Smith's test: The urine is overlayed with tincture of iodine, diluted with 9 times its volume of alcohol. An emerald green ring at the zone of contact shows the presence of bile pigments. 3. Franklin's bilirubin test: Ten drops of urine are dropped on a tablet made of plaster of paris and containing barium chloride. Two drops of Fouchet's reagent (one-half strength) are added to the surface of the tablets. The presence of bilirubin in the urine is denoted by the appearance of a color ranging from slight bluish-green to deep green. 4. Ictotest: Five drops of urine are placed on an asbestos–cellulose test mat. An Ictotest reagent tablet, containing *p*-nitrobenzenediazonium–*p*-toluenesulfonate, sulfosalicylic acid, sodium bicarbonate, and boric acid, is placed in the center of the moistened area. Two drops of water are dropped on the tablet, allowing the water to run down the sides of the tablet. If the test is positive, the mat around the tablet turns purple.

In addition, 46 urine specimens of 23 control patients with no signs of jaundice and/or liver disease, who had albumin, blood, sugar, or ketone bodies in their urine or had been on different medications, were tested by Ictotest alone to investigate the effect of various urine contents on the Ictotest reaction. Ictotest was found to be the most sensitive. The simple and economical Rosenbach test came close to the sensitivity of Ictotest. The height of the indirect serum bilirubin and the amount of bile in the urine were not always parallel.

SURGERY

Palliative Treatment of Obstructing Processes in the Esophagus and Cardia with Intubation. E. Skielboe. Ugesk. laeger **120**:1222-1225 (Sept. 11) 1958 (In Danish) [Copenhagen].

In cancer of the esophagus and cardia, where the possibility of radical operation is excluded and marked difficulty in swallowing even liquid food is not lessened by roentgen-ray treatment, intubation according to Souttar's method seems to be the most satisfactory treatment, except in tumors in the pars superior of the esophagus. In cases in which the tumor is soft or is longer than Souttar's tube, Mousseau-Barbin's plastic tube is useful and requires no special equipment for application. Palliative intubation was carried out in 51 patients with obstructing and mainly malignant processes in the esophagus and cardia—in 41 according to Souttar and in 10 with the Mousseau-Barbin plastic tube. The average time of survival was only 4 or 5 months, but palliative intervention was justified. Souttar's method should be applied generally in preference to gastrostomy, and in suitable cases it is admirably supplemented by Mousseau-Barbin's plastic tube.

Treatment and Prophylaxis of Acute Cardiovascular Insufficiency During Mitral Commissurotomy. S. I. Smelovsky, T. M. Barbinyan and Y. M. Panova. Khirurgiya **34**:21-26 (no. 8) 1958 (In Russian) [Moscow].

Acute cardiovascular insufficiency requiring intra-arterial blood transfusion occurred in 46 patients, of a total number of 135, during a mitral commissurotomy performed for stenosis of the left mitral valve. In patients with this complication hypoxia was successfully treated by intra-arterial blood transfusion. Acute cardiovascular insufficiency is caused by the operation itself and by hemorrhage from the left auricular appendage. The weakness of the left ventricle adapted for minimal blood filling also plays a certain role. After dilatation of the mitral orifice this weakness of the left ventricle may give rise to acute insufficiency. Prophylactic intra-arterial blood transfusion is recommended for the prevention of acute cardiovascular insufficiency. Employment of this method, with the administration of epinephrine, during a commissurotomy prevents acute cardiovascular insufficiency. The authors consider that the best site for transfusion is the arteria tibialis posterior. At times the intra-arterial blood transfusion causes pain in the course of the main blood vessels of the lower extremity and paresis of the peroneal nerve. Development of acute cardiovascular insufficiency in 40% of cases of mitral commissurotomy justifies the employment of prophylactic intra-arterial blood transfusion in all cases of surgical treatment of stenosis of the mitral valve.

Mediastinal Chemodectoma. T. J. Madden. Ann. Surg. **148**:943-950 (Dec.) 1958 [Philadelphia].

The author reports on a 28-year-old pregnant woman with a mediastinal tumor of aortic body origin which was detected in a routine chest roentgenogram taken in the 6th month of pregnancy. Bronchoscopic examination showed downward displacement of the right upper lobe bronchus. A right-sided thoracotomy was performed, and the entire tumor was removed with a short segment of the innominate artery. Three months later the patient was delivered of a normal female infant. Nineteen months after removal of the tumor the

patient was alive and apparently free of disease. Microscopic examination of the operative specimen revealed an extremely vascular tumor, consisting of polyhedral cells with finely granular eosinophilic cytoplasm. The cells were arranged in groups separated by thin fibrous septums. Throughout the tumor there were small clumps of iron-containing, golden-brown pigment. Ten additional cases of carotid-body tumors arising in the mediastinum and in relation to the base of the heart and great vessels were collected from the literature and summarized, together with available recent follow-up data on patients who were living at the time of the original reports.

This summation of experience with mediastinal chemodectomas, together with the known facts about the related and more common tumors of carotid bodies and jugular glomera, is the basis for the following tentative conclusions about the natural history of the tumors. Mediastinal chemodectomas are slow-growing tumors which rarely metastasize but may recur locally after incomplete excision. They occur anywhere in the mediastinum, not necessarily in the usual sites of normal aortic glomera. They may be associated with tumors of similar type in other locations. Surgical treatment may be difficult, and a conservative approach seems to be warranted. Treatment by x-ray is not likely to be effective.

A Report Upon a Patient Five Years Following Resection of the Abdominal Aorta for Recurrent Carcinoma. S. W. Moore. Surg. Gynec. & Obst. **107**:709-711 (Dec.) 1958 [Chicago].

The patient was a woman who was 56 years old when she was admitted to the New York Hospital in May, 1952, because of a mass in her abdomen. On Jan. 11, 1949, in another hospital, she had been subjected to an anterior resection of the sigmoid colon for adenocarcinoma with perforation. The abdominal mass detected 3½ years later was firm, fixed, rounded, and 10 cm. in diameter, and lay in the left lower quadrant. At operation on May 21, 1952, a large tumor, 10 by 6 by 4 cm., was found lying between the aorta and the sigmoid colon. Although not fixed, the tumor was adherent to the aorta and to the left common iliac artery. The left ureter entered the mass. There were no metastases in the liver or lymph nodes along the aorta. The tumor was thought to be a local recurrence of the sigmoid carcinoma resected 3½ years previously. To remove the mass, it was necessary to resect en bloc the aorta, both common iliac arteries, and the left ureter together with the tumor. A homograft of abdominal aorta with bifurcation was inserted in the defect by end-to-end anastomosis.

Immediately after operation, there was excellent bilateral pulsation in the femoral and dorsalis pedis arteries. The gross specimens, as well as microscopic sections, showed recurrent carcinoma invading, but not yet penetrating, the lumen of the aorta. Twenty-five days later, on June 16, 1952, the sigmoid colon and left kidney were removed. Four months later, on Nov. 17, a cholecystectomy for chronic cholecystitis with cholelithiasis was carried out without incident. On Oct. 20, 1954, 2 years later, a bilateral subtotal thyroid lobectomy was performed for nontoxic nodular goiter. Now 5½ years have elapsed since resection of the secondary carcinoma, and this patient is quite well save for minor complaints. There is no evidence of cancer, and no loss of weight. Both femoral and dorsalis pedis vessels on both sides are readily palpable with good pulsations.

Prescalene Node Biopsy. K. Cruze, R. F. Hoffman, W. B. Hayden and F. X. Byron. Ann. Surg. **148**:895-898 (Dec.) 1958 [Philadelphia].

The authors report on 151 patients, between the ages of 23 and 81 years, on whom 164 prescalene lymph node biopsies were performed with the aid of local anesthesia in the section of thoracic surgery of the Veterans Administration Center in Los Angeles between January, 1953, and October, 1957. A conclusive tissue diagnosis was rendered in 51 (31.1%) of the 164 biopsies. This procedure may prevent needless operation. The indications should include suspected bronchogenic carcinoma or abnormal pulmonary shadows. Bilateral biopsy is indicated in some instances. Prescalene lymph node biopsy yielded positive results in 26 (38.2%) of 68 cases of bronchogenic carcinoma proved by autopsy, clinical, or other ancillary methods. A compilation of the results of prescalene lymph node biopsies reported by other workers and collected from the literature revealed about 30% positive biopsies for all lesions. Complications did not occur when the biopsy was performed with the patient under local anesthesia.

Portacaval Anastomosis: A Study of 12 Pre- and Post-operative Cases. L. Leger and R. Roy-Camille. Presse méd. **66**:1673-1676 (Oct. 29) 1958 (In French) [Paris].

Twelve patients with cirrhosis, who had undergone portacaval anastomosis, were followed up for a period of 6 to 18 months after operation. Portal hypertension returned to normal values in 3 patients, it was decreasing over several months in 8 patients, in 2 of whom it began to increase after a while; and it remained unchanged in 1 patient who died of hemorrhage a year after the operation. Another patient died in hepatic coma 21 months after the operation. Clinical improvement, potency of the anastomosis, and cessation of hemorrhage were observed in this series of patients after the surgical treatment. Disappearance of the blood reflux followed the operation, but it returned in a

slight degree in 3 patients. Roentgenologic examination of esophageal varices in 7 patients after the operation showed that they remained unchanged in 1 patient and diminished in 6. Liver function improved in 1 patient, remained unchanged in 2, and deteriorated in 4.

Contributions to Surgical Treatment of Portal Hypertension. M. A. Khelimsky. Khirurgiya **34**:10-14 (no. 8) 1958 (In Russian) [Moscow].

Splenectomy with simultaneous omentohepatofixation and omentorenopexis was employed by the author in patients with the syndrome of portal hypertension and with thrombophlebitic splenomegaly and splenogenic cirrhosis of the liver. He operated on 11 patients who were admitted to the clinic because of hemorrhages due to varicose veins of the esophagus. There were 6 men, 4 women, and a 13-year-old girl. After the operation a normal blood picture was reestablished in all the patients, and thrombopenia, ascites, and hemorrhages disappeared. Ten patients have resumed their work. One patient in whom omentohepatofixation alone was performed without omentorenopexis died 1½ years after the operation as a result of thrombosis of a branch of the superior mesenteric artery.

Emergency Surgery for Severe Upper Gastrointestinal Hemorrhage: An Analysis of Sixty-Four Cases. W. E. Switzer and W. W. Nichol. A. M. A. Arch. Surg. **77**:843-850 (Dec.) 1958 [Chicago].

This report is concerned with patients who were operated on as emergencies because of severe upper gastrointestinal bleeding. The case series was accumulated during the years from 1950 through 1957 at a large Army hospital and includes active-duty military personnel and their dependents, retired military personnel, and Veterans Administration beneficiaries. Not included are the many patients whose bleeding ceased with conservative treatment or those persons who were operated on electively after a bleeding episode. During the period mentioned, 353 patients entered the hospital with upper gastrointestinal bleeding. Sixty-four (18.1%) were operated on. All but 2 of these 64 patients were men. The ages of the patients ranged from 17 to 74 years; 33 were under, and 31 were over, 50 years of age. There was an increase in the number of patients requiring surgery for gastrointestinal bleeding in the fall. The month of November alone accounted for 12 (18.8%) of the entire group, in contrast to July when no operations were done for gastrointestinal bleeding during the entire 8-year period. Both hematemesis and melena occurred in 44 patients, melena only in 13, and hematemesis only in 7.

After commenting on preoperative hemoglobin and hematocrit values, on transfusion requirements, preoperative endoscopy, and roentgenoscopy, the authors state that 56 of the 64 patients were treated by subtotal gastric resection, and 2 by total resection. The remaining 6 patients were treated by one of the following: ligation of the bleeding gastric ulcer; suture of a stomal ulcer; exploration and pyloroplasty; suture and packing of ulcer; exploration only; and suture of laceration at the gastric cardia associated with repeated vomiting (Mallory-Weiss syndrome). The following points are emphasized: 1. These patients benefited from a combined medical-surgical evaluation of their problem. 2. The results of the early diagnostic procedures of endoscopy and upper gastrointestinal x-rays appeared to justify the effort required, without undue risk to the patients. 3. Blood transfusion requirements in these patients should be thought of in terms of one-half to several times the patient's estimated normal blood volume. 4. Although the mortality rate in the above-50 age group was more than triple that of the below-50 age group, it was also true that the lives of 24 of the 31 patients above 50 years were prolonged by surgical intervention. 5. Recurrent bleeding and sepsis were the complications most frequently associated with death.

Favorable Postgastrectomy Results in Billroth II Patients with a Small Stoma. J. J. McCaughan Jr. and R. F. Bowers. A. M. A. Arch. Surg. **77**:837-842 (Dec.) 1958 [Chicago].

The Billroth 2 type of gastric resection has been widely accepted, because it has the lowest peptic ulcer recurrence rate of any of the procedures in use, while the mortality and immediate morbidity rates are comparable. However, the late postgastrectomy findings of weight loss, diarrhea, and the dumping syndrome with accompanying weakness are believed to be more frequent than with other procedures, notably gastroenterostomy and the Billroth 1 procedure. The postoperative study of patients who have undergone the Billroth 2 type of gastric resection suggests that the symptoms are due to loss of the pyloric sphincter and stomach, which is usually associated with rapid emptying of the stomach. This sudden flow of food and fluid into the jejunum must be slowed down. To test the validity of this concept, the authors deliberately formed a small stoma in the Billroth 2 operation. The purpose of the small stoma was to retard the gastric emptying. Roughly, 1.5 to 2.5 cm. has been the selected size of the small stoma, although this cannot be accurately measured. A stoma of 2.5 to 6 cm., or larger, is regarded as large by the authors. They found some large stomas of the Pólya type to be from 4 to 6 cm. in diameter. The measurement of the stomas is not accurate, but is estimated by the surgeon with finger and thumb.

The authors compared the results obtained by Billroth 2 gastrectomy in 100 patients with small stomas with those in 100 with large stomas. Follow-

up studies by personal interview revealed that the postgastrectomy syndrome was reduced approximately by one-half in the small-stoma group as compared with the control group. Weight loss was reduced from an average of 9.83 lb. in the control group to 3.84 lb. in the small-stoma group. Weakness, which seemed to be the commonest and severest complaint of the control group, was decidedly better in the small-stoma group. Diarrhea was approximately equal in frequency in the two groups. Subtle distinction in postcibal symptomatology in the two groups did not seem feasible in this series. If there was doubt about the presence of postgastrectomy symptoms, the authors used the oral glucose intake test (250 cc. of 50% glucose by mouth), which proved to be very practical and produced the symptoms if the patient had really experienced the postgastrectomy syndrome. It was often difficult to separate psychosomatic symptoms from the actual ones, but the glucose test was helpful in these instances. A small number of patients experienced the dumping syndrome even when stomal obstruction was present.

Making the partially obstructing stoma proved difficult. At the end of the operation, the surgeon often could not predict the degree of stomal obstruction that would follow. The best results were obtained from stomas that would just admit one small finger.

Gastric Polyps. K. Kettunen. Ann. chir. et gynaec. Fenniae **47**:300-312 (no. 4) 1958 (In English) [Helsinki].

Of 14,566 patients who underwent roentgenologic examinations in the department of roentgenology of the Maria Hospital in Helsinki between 1948 and 1955, gastric polyps were detected in 37. The author reports on these 37 patients (15 men and 22 women), whose ages ranged from 32 to 88 years, with an average age of 60.2 years. Epigastric distress and pain were the most prominent and significant complaints. Achlorhydria was found in 19 of 21 patients tested. Four patients had pernicious anemia. Malignant transformation was present in 3. Thirteen of the 37 patients had single gastric polyps, 4 had 2 polyps, and 20 had 3 or more. Generalized polyposis was present in 3 patients.

Treatment in 26 of the 37 patients was conservative, while partial gastric resection was performed on 7, exploratory operation on 1, simple excision on 2, and subtotal gastric resection on 1. It is suggested that roentgenologic examinations, with the aid of barium as contrast medium, be used in establishing a diagnosis of gastric polyps; gastroscopic examination should be used as a supplement to the roentgenographic study, since it may reveal polyps overlooked by the latter method and vice versa. If malignant disease cannot be determined on the basis of gastroscopic or roentgenologic examination, an exploratory operation is recommended.

Excisional Treatment of Aneurysm of Celiac Artery. H. B. Shumacker Jr. and H. Siderys. Ann. Surg. **148**:885-889 (Dec.) 1958 [Philadelphia].

Of 35 patients with aneurysm of the celiac artery, whose cases have been reported in the literature, 31 died of rupture. None of the patients was treated successfully by surgery. This fact prompted the authors to present the case of a patient with multiple arteriosclerotic abdominal aneurysms, who has recently been treated successfully by surgery. The patient was a 41-year-old woman who was admitted to the department of surgery of the Indiana University Medical Center in Indianapolis in August, 1957. Aneurysms of the celiac axis, the splenic artery, and both common iliac arteries were excised. Ischemia of the stomach and liver followed temporary occlusion of the celiac artery and was obviated after resection of the celiac aneurysm by anastomosis of the remaining stump of the celiac artery and the main hepatic artery. Aortic-iliac continuity was restored by insertion of a bifurcation graft. The patient had an uneventful convalescence and was discharged on the 12th postoperative day. In view of the extent of her arteriosclerotic disease and the high normal level of her serum cholesterol, she was placed on a low-cholesterol and low-fat diet. When she was seen 3 months later, she was well and had been working full time. The liver edge was not palpable, and the peripheral pulses were excellent.

Congenital Pyloric Stenosis Treated by the Ramstedt Operation: A Review of 1,018 Cases. S. Feggetter. J. Internat. Coll. Surgeons **30**:696-700 (Dec.) 1958 [Chicago].

The author reports on 1,018 children with congenital pyloric stenosis, who underwent the Ramstedt operation in Newcastle, England, between 1940 and 1956. Seventeen children died, representing a mortality rate of 1.6%. The operative and postoperative complications are listed, and a typical case in a 4-week-old boy is described. Medical accounts refer occasionally to congenital pyloric stenosis from the year 1700 onward, but the first accurate description of the disease was presented by Hirschsprung in 1887. All the signs and symptoms result from obstruction due to a pyloric tumor, which is caused by true hypertrophy of the circular muscle of the pyloric canal. The development of the tumor depends on the presence of a recessive gene; it is to be expected, therefore, that the incidence of the anomaly will increase. It now occurs in approximately 3 of each 1,000 live births. In 1946, the over-all mortality rate in England and

Wales was 20%. The differential diagnosis includes infectious vomiting, pylorospasm, and the intestinal atresias. The treatment of choice is the Ramstedt operation performed with the aid of open ether anesthesia. It has been observed that, when children in a given area have been treated by one or two surgeons interested in this type of work, with the assistance of a pediatric team and a skilled anesthetist, the results of the Ramstedt operation have been substantially improved.

Surgical Treatment of Disease of the Prostate in Patients with Diabetes Mellitus. H. Eufinger and D. Borm. Beitr. klin. Chir. **197**:11-15 (no. 1) 1958 (In German) [Munich].

The authors report on 12 men, between 56 and 81 years, with disease of the prostate and diabetes mellitus who were operated on at the surgical clinic of the University of Kiel, Germany, between 1947 and 1956. Of the 12 patients, 9 had adenoma of the prostate, and 3 had carcinoma of the prostate. Ten patients underwent electroresection, and 2 were subjected to suprapubic prostatectomy according to Freyer. Four of the 10 patients required a second resection, and, therefore, 16 operations were performed on the 12 patients. The blood sugar values of the patients varied between 122 and 257 mg. per 100 cc., and the amounts of sugar excreted in the urine varied between 0.59 and 14.7 Gm. The diabetes mellitus was discovered in 3 patients only after admission to the surgical clinic, and its duration in 4 patients varied between 17 and 23 years. Six patients were hospitalized because of acute retention of urine, with 300 to 2,000 cc. of fluid contents of the bladder, and the other 6 were hospitalized because of dysuria and pollakiuria. One of the patients died on the third postoperative day of pulmonary embolism. The remaining 11 patients were discharged from the hospital, and 10 were followed up after their discharge. One died 8 days later at home, one who had carcinoma of the prostate died 4 years after the operation, and one died 2 years after the operation. The remaining 7 patients are still alive and free of complaints of micturition. Four patients no longer require treatment with insulin. In 3 of these, the disease of the prostate caused a latent diabetes mellitus in patients of advanced age to become manifest, but the diabetes became latent again after surgical treatment of the prostate. Three patients are still receiving insulin, but the diabetic disturbance of metabolism is controlled by the drug.

These findings show that diabetes mellitus does not represent a contraindication to surgical intervention in patients with disease of the prostate. It seems that the type of the surgical procedure and the preoperative and postoperative administration of antibiotics and chemotherapeutic preparations, respectively, are of far less importance in the surgical treatment of diabetic patients with disease of the prostate than the preoperative control of the diabetic metabolism by the internist.

Importance of Early Operation in Congenital Atresia of the Extrahepatic Bile Ducts: Report of 10 Proved Cases. G. E. Schnug. Ann. Surg. **148**:931-936 (Dec.) 1958 [Philadelphia].

The author reports on 10 newborn infants with obstructive jaundice caused by congenital atresia of the extrahepatic bile ducts. Five of these had atresia of the extrahepatic bile ducts which was surgically correctable. Two of the 5 were operated on, one successfully, at the age of 2 months, and the other unsuccessfully at the age of 6 months; the other 3 patients were not operated on, but autopsy revealed that the anomalies had been correctable. Marked liver changes secondary to atresia of the bile ducts were observed on autopsy. Even the one infant who was operated on successfully had advanced cirrhosis of the liver. She survived several hemorrhages and reached the age of 3 years, at which time it was felt that her vessels were large enough so that a splenorenal shunt could be made. Splenectomy also was done, and the patient is now a normal 5½-year-old girl. Her liver function has gradually improved over a period of years. In the 291 patients with congenital atresia of the extrahepatic bile ducts, whose cases were collected from the literature, the cause of death was most frequently failure of the liver. The atresia was surgically correctable in 68, and only 24 of these were reported as cured. It was also noted that almost all successfully treated patients were operated on when they were less than 2 months old.

Available diagnostic measures are inadequate in differentiating the various types of obstructive jaundice in the newborn infant. The reported data show that irreversible changes in the liver do occur early in patients with biliary atresia. Exploration within the first months of age has been recommended. Anastomosis between the extrahepatic biliary tree and the duodenum is the simplest and probably the procedure of choice. It seems quite definite that the liver damage and the complications and sequelae resulting from the damage are the cause of the poor results in the treatment of patients with correctable biliary atresia.

Antibiotic Therapy: Adverse Effects in Acute Appendicitis Before Diagnosis. R. B. Dietrick, C. W. Byrd and J. A. Lawson. Ann. Surg. **148**:985-990 (Dec.) 1958 [Philadelphia].

Of 46 patients with acute appendicitis who were admitted to the surgical service of the Veterans Administration Hospital in Richmond, Va., between 1955 and 1957, 5 (10.9%) had been treated with antibiotics or sulfonamides before a diagnosis was established or before an operation was performed.

The authors believe that this therapy obscured the symptoms of appendicitis and thereby delayed and made the diagnosis more difficult. As a result of being unable to reach an early diagnosis, the morbidity, length of hospital stay, and expense of hospitalization were greatly increased. The experience with these patients indicates that appendicitis treated with antibiotics may lead to 2 different clinical pictures: (*a*) patients who are obviously ill, who have masked and atypical symptoms, and who require exploration on the basis of the clinical picture and (*b*) patients whose symptoms are so completely masked that no specific diagnosis can be made, who do not appear to require exploration on the basis of their clinical findings, and who settle into a state of chronic disability which may extend over many months, with occasional exacerbations.

The 5 patients treated with antibiotics had a large number of complications, either directly or indirectly, due to their primary disease. In one patient a severe wound infection developed, and he also required a skin graft to an ulcer caused by extravasation of arterenol, which was given to correct persistent severe hypotension postoperatively; an abscess arose in his McBurney scar 18 months after operation. Intestinal obstruction was caused in another patient by a volvulus about the point of adherence of the inflamed appendix to the terminal ileum. In a third patient persistent rectal stenosis occurred at the site of adherence of the appendix to the rectum. In still another patient gross hematuria was caused by genitourinary manipulations, and intestinal obstruction due to a great number of postoperative adhesions, resulting from chronic inflammation over a period of many months, required reoperation. Patients with undiagnosed abdominal pain should not receive antibiotics until appendicitis can definitely be excluded as a diagnosis. In patients admitted with abdominal pain in whom the symptoms are atypical, the examining physician should have a high index of suspicion that the patient may have received antibiotic therapy and should closely question the patient concerning this possibility. When the patient gives such a history, early exploration is indicated despite the paucity of physical findings.

Differential Diagnosis of Mitral Pathology. B. V. Petrovski and V. V. Zaretski. Vestnik khir. **81:**28-33 (Nov.) 1958 (In Russian) [Leningrad].

Electrokymography (study of pulsations of various segments of the peripheral contour of the heart) has been successfully applied in the diagnosis of heart anomalies, 128 commissurotomies having confirmed its findings. The left atrium electrokymogram reveals best of all the peculiarities of mitral defects. The left atrioventricular valve stenosis is reflected by an inhibited and prolonged systole of the left atrium, the electrokymogram showing a diastolic plateau. After the atrial systole is over, a mitral valve insufficiency is disclosed by a regurgitation reflux indentation on the electrokymogram of the left atrium during the systole of the left ventricle. The existence of mixed mitral defects is evidenced on the electrokymogram by elements of left venous orifice stenosis and mitral valve insufficiency, the more advanced anomaly being revealed by the prevalence of its characteristics.

Clinical and Functional Assessment of Surgical Treatment of Mitral Stenosis: A Follow-Up. A. L. Izbinski and T. G. Blestkina. Vestnik khir. **81:**33-40 (Nov.) 1958 (In Russian) [Leningrad].

Treatment of 110 patients by mitral commissurotomy is evaluated in a follow-up ranging from 6 months to 4 years. A favorable outcome was found in 86% of the cases. An adjuvant classification of third-degree competence of the "second barrier," devised by Izbinski and his co-workers, was added to the usual classification of blood circulation impairment in the preoperative and the postoperative assessment of the patient's condition. By "second barrier" the authors refer to the complex of pathological changes in the pulmonary parenchyma and in the pulmonary circulation developing on the basis of mitral stenosis. The unfavorable results were found to depend on (1) a failure of the commissurotomy itself, (2) a rather late recrudescence of rheumatic infection, (3) marked dystrophic myocardial changes, (4) intercurrent diseases, and (5) clear-cut symptoms of the "second barrier" complex before the operation. This adjuvant classification gives a more reliable appraisal of the patient's condition before surgery and has an important significance for the prognosis of late results. A fourth-degree circulatory impairment does not preclude surgical treatment of mitral stenosis, because an effective commissurotomy is often followed by a marked improvement in the patient's condition and even by a partial return to work fitness.

Indications and Contraindications for Shunt Operations in Portal Hypertension. S. Brandstaetter. Harefuah **55:**242-243 (Nov. 16) 1958 (In Hebrew with English Summary) [Tel-Aviv, Israel].

According to Brandstaetter, a brief survey of the newer techniques indicates that splenoportography and measurement of the splenic pressure are the best methods available for determining whether portal hypertension is the cause of esophageal varices in a given case and whether portal hypertension is due to intrahepatic or extrahepatic block. In a patient with bleeding varices and portal hypertension, intrahepatic block is a clear indication for a shunt operation. Laboratory tests suggested by Linton proved to be a relatively reliable index in the selection of patients for portacaval shunt. A

patient with repeated hemorrhages and borderline liver function tests is a bad risk for splenorenal shunt, and portacaval shunt is contraindicated. Uncontrollable ascites remains a contraindication to shunt procedures until more reliable statistical material has been gathered. As even in good-risk patients the operative mortality is still about 10%, the advisability of prophylactic shunt in patients with cirrhosis and varices who have never bled is still a moot problem.

The Use of Controlled Hypothermia for the Prevention of Ischemic Renal Damage Produced by Cross-Clamping of the Thoracic Aorta: Experimental Observations. R. Benvenuto and M. Serratto. Minerva med. **49**:3948-3952 (Oct. 20) 1958 (In Italian) [Turin, Italy].

A study on hypothermia induced to protect the kidney against ischemic damage due to occlusion of the thoracic aorta is reported. The experiment was carried out on 18 male and female dogs, each having a body weight of 15 to 20 kg., divided into 2 groups. The first group was composed of 12 animals, 6 used as controls and operated on at a normal temperature and 6 operated on under hypothermia; a series of biopsies of the kidney was carried out in these animals after the operation. The second group was composed of 6 animals, 2 used as controls and operated on at a normal temperature and 4 operated on under hypothermia. Anesthesia was induced in all dogs with intravenous injections of Nembutal, 30 mg. per kilogram of body weight, and respiration was controlled by means of tracheal intubation and of a mechanical respirator. In the dogs subjected to hypothermia, the temperature was reduced to 32 C (89.6 F) by means of thermal blankets at the moment that the thorax was being opened, and to 28 C (82.4 F) when occlusion of the aorta by cross-clamping took place. Normal temperature, 37 C (98.6 F), was restored by introducing hot water in the thermal blankets. Occlusion of the aorta for one hour caused necrosis of the convoluted tubules of the kidney in all the animals used as controls. Biopsy performed soon after the restoration of normal temperature, and 24 and 36 hours after the operation, revealed no necrosis of kidney tissues in the animals operated on under hypothermia.

Necrosis of the proximal tubule, already on the way to recovery, was noticed in one animal on which biopsy was performed one week after the intervention. This animal also presented signs of spontaneous nephritis. Kidney function was seriously impaired in all the control dogs soon after the operation; it improved later, but it never returned to the condition it was before operation. In the dogs operated on under hypothermia, kidney function was slightly but temporarily impaired. Normal values were obtained in clearances carried out 1 or 5 weeks after the operation.

Rheumatoid Tenosynovitis: Diagnosis and Treatment. T. A. Potter and J. G. Kuhns. J. Bone & Joint Surg. **40A**:1230-1235 (Dec.) 1958 [Boston].

The authors report on 154 patients with rheumatoid tenosynovitis who were treated at the Robert Breck Brigham Hospital in Boston and were followed for periods exceeding one year. Of these, 65 with only small swellings were treated conservatively with heat and support. Thirty of these have been cured, i. e., the tenosynovitis has disappeared and has not recurred. In 10, the lesion has become smaller but is still present; the remaining 25 did not respond to this method of treatment. Thirty-five patients with circumscribed lesions not larger than 1 in. in diameter were treated by injection of hydrocortisone, repeated at 2-week intervals; 15 of these showed complete disappearance of the swelling, the condition of 5 was improved, and 15 were therapeutic failures. In 30 patients with masses on the tendons larger than 1 in., the lesions were excised; 20 patients were relieved completely and had no recurrence, 3 had a slight recurrence of the swelling, and 7 had an early recurrence of the lesion. Tendon repairs, including resuturing, grafting, and transferring of tendons, were performed on 24 patients; in 10 of these the operation restored good function, improvement in function was observed in 2, and 12 were therapeutic failures.

Rheumatoid tenosynovitis is a common complication of rheumatoid arthritis; its slow, nonpainful development often results in failure of recognition and diagnosis. This lesion is found most commonly on the dorsum of the wrist, involving the extensor tendons. Diagnosis can be established only by microscopic examination of the diseased tissue. It can be suspected when swelling appears in and upon the tendons in the presence of rheumatoid arthritis. Treatment in the early stage should include heat, support, and relaxation of the tendon. It may be supplemented by injections of hydrocortisone into the mass every 2 weeks. When the swelling becomes large, excision of the diseased tissue as completely as possible is advised. Rupture of tendons requires surgical repair. No relationship could be established between rheumatoid tenosynovitis and Quervain's disease and snapping finger.

The Value of Shunt Operations for Portal Hypertension. D. Erlik. Harefuah **55**:233-238 (Nov. 16) 1958 (In Hebrew with English Summary) [Tel-Aviv, Israel].

Of 17 shunt operations for portal hypertension, 10 were splenorenal shunts and 7 were portacaval shunts. Two of these shunt operations performed for Budd-Chiari syndrome were not analyzed. Shunting was performed for cirrhosis of the liver in 13 patients, and for extrahepatic block in the remaining 2. Of 6 patients on whom portacaval

shunt was performed, 2 died within 10 days of the operation, but in these the liver function tests indicated that death was caused by hepatic insufficiency leading to coma. The other 4 patients are in satisfactory condition from 1 to 3 years after the operation; the severe preoperative hemorrhages did not recur. No deaths attributable to the operation occurred in 9 patients undergoing splenorenal shunts, but 3 of these patients died because of recurrent esophageal bleeding 2 weeks, 6 months, and 2 years, respectively, after the operation. The shunt was found to be thrombosed in all fatal cases. The progress of the other 6 patients was satisfactory with no recurrence of bleeding.

On the basis of these observations and of literature reports, the author concludes that shunt operations are serious procedures owing to the dangers of immediate and delayed complications. The decision to perform a shunt operation requires thorough study of the individual patient, but there should be no wavering if operation is required. In case of severe hemorrhage from esophageal varices, a shunt should be performed before another bout of bleeding may be fatal.

The choice of shunt is a source of controversy. The portacaval shunt is the best as regards function and, therefore, the most reliable in preventing hemorrhage, but for this type liver function tests must at least be fair. When the liver tests are seriously impaired, the splenorenal shunt is preferable, although it is prone to closure by thrombosis. This type of shunt gives excellent results in extrahepatic block. Shunt operations should not be performed to prevent anticipated hemorrhage. The only exceptions are cases in which splenectomy is performed for congestive splenomegaly with severe hypersplenic phenomena. In these cases the splenic vein should be saved from thrombosis by performing a "prophylactic" splenorenal shunt. When severe and repeated hemorrhages from esophageal varices occur at short intervals, a Blakemore tube should be introduced into the esophagus to stop the bleeding. Then a suitable shunt is constructed with the balloon still in place. One or 2 days after the operation the balloon can be removed without danger of further bleeding.

Antibiotics for Colon Surgery. I. Cohn Jr. Gastroenterology **35**:583-591 (Dec.) 1958 [Baltimore].

Evaluation by standardized methods of 28 agents for intestinal antisepsis permitted their division into recommended and less satisfactory groups. All the groups recommended for general use in intestinal antisepsis are combinations of neomycin with another poorly absorbed agent. A clinical trial of a triphasic antibiotic administration program was undertaken in patients who were subjected to surgical intervention on the colon; these patients were selected from the Louisiana State University surgical service at Charity Hospital of Louisiana and from 4 other hospitals in New Orleans. The 3 phases of the program were as follows: (1) preoperative preparation with a combination of 1 Gm. of neomycin and 200 mg. of tetracycline (Achromycin) given every hour for 4 hours, then every 6 hours for a total of 72 hours; (2) intracolonic instillation of a powder containing 250 mg. of tetracycline and 1.25 Gm. of neomycin into the lumen of the colon whenever the colon was opened for any reason; and (3) postoperative intraluminal injection of a mixture of 150 mg. of tetracycline and 750 mg. of neomycin, dissolved in 10 cc. of sterile saline solution; this mixture was injected 3 times daily for the first 5 postoperative days through a plastic tube, which was inserted into the colon proximal to the point of anastomosis of colotomy and exteriorized through a stab wound.

Between July 1, 1955, and Dec. 31, 1957, 200 patients were evaluated on this antibiotic program for colon surgery. No cases of pseudomembranous enterocolitis were observed, and the absence of fistulas and of peritonitis in the 67 patients who received postoperative treatment through the plastic tube encouraged further study of this form of therapy. Complications were not completely eliminated in these surgical patients, though, and it should not be expected that any amount of antibiotic therapy would eliminate all complications, nor should such therapy replace sound surgical principles. Clinical experience with these 200 patients over 2½ years has substantiated the experimental evidence that a high concentration of antibiotics should be maintained within the lumen of the intestine before, at the time of, and after surgical intervention on the colon.

Arthrogryposis Multiplex Congenita. N. G. Mead, W. C. Lithgow and H. J. Sweeney. J. Bone & Joint Surg. **40A**:1285-1309 (Dec.) 1958 [Boston].

During a period of 31 years, 68 patients with arthrogryposis multiplex congenita were treated at the Shriners' Hospital for Crippled Children in Chicago. The authors report on 40 of these, who were examined and treated and on whom close follow-up studies were carried out. Twelve patients were followed from infancy into adulthood. All 4 extremities were involved in 20 patients, both lower extremities in 11, both lower and one upper extremity in 7, both upper extremities in 1, and one lower and one upper extremity in 1. The causation and pathology of arthrogryposis are not well understood, and there is no general agreement concerning them. Until the true nature of this congenital disorder, which is characterized by multiple rigid joint deformities, is known, there is little advantage in using other terms for the condition. The occurrence of the disease in one member of each of 4 sets of identical twins, 2 of which are in this

series, seems to exclude hereditary factors as the cause and to cast doubt on theories of intrauterine mechanical, circulatory, or toxic causes. The negative family histories further tend to exclude the theory that heredity is a cause.

The primary pathological site may be either in the spinal cord or in the muscles. It is believed that the fibrosis around the joints and in the subcutaneous tissues is a part of the pathological process and not merely secondary to intrauterine inactivity. Mental deficiency is infrequent in patients with arthrogryposis. When present, it does not appear to be more than coincidental. Only 2 of the 40 patients were considered to be below normal in intelligence; one of these had cerebral palsy also, and it was felt that the mental deficiency was related to this condition. The joint deformities are difficult to correct and to maintain in correction. Function may be poor because of stiffness or lack of muscle power even when the deformity has been overcome. Stiff joints must be placed in the position of function, and unstable limbs must be braced for weight bearing. If these things are accomplished, results will be satisfactory. Patients with arthrogryposis, even though severely handicapped, generally make a satisfactory adjustment and live successful lives. Severe pain is not often present despite the poor mechanics many of these people must endure.

Congenital Pseudarthrosis of the Tibia. H. B. Boyd and F. P. Sage. J. Bone & Joint Surg. **40A**:1245-1270 (Dec.) 1958 [Boston].

The authors report on 9 girls and 6 boys with congenital pseudarthrosis, who were operated on at the Campbell Clinic-Hospital in Memphis, Tenn. Of the 15 patients, 7 who were treated between 1941 and 1948 have reached skeletal maturity, and end-results are reported not only regarding treatment but also regarding social and economic status. The remaining 8 were operated on after 1948, and since none of these have reached skeletal maturity, they cannot be included in an end-result study. All 7 patients in the first group had repeated reconstructive operations: 1 of these was a surgical failure because treatment resulted in below-the-knee amputation; 3 had moderate results, 2 of them requiring braces and 1 requiring a shoe elevation; 3 were operated on successfully, having no longer complaints referable to the lower extremities. From a social and economic point of view treatment was successful in 6 of the 7 patients. The one surgical failure was a social and economic success.

There are two distinct types of congenital pseudarthrosis of the tibia. In the first, a cystic defect, with or without fracture, is present, and the pathological findings resemble those in fibrous dysplasia. The second shows sclerosis and tapering of the bone ends, probably due to a constricting band of fibrous tissue. In this type, union is more difficult to secure. The causative factors are still undetermined, but congenital pseudarthrosis is probably due to a maldevelopment of the mesodermal structure during the 5th week of fetal life, with an associated abnormality occurring in the nerve pathways to the affected leg. Early surgical treatment before the development of marked deformity is advised. In the first type, the cyst should be curetted and the defect filled with bone chips; additional bone grafting may or may not be necessary. In the second type, a wide resection of the constricting band of pathological soft tissue should be done, combined with suitable bone grafting and adequate internal and external fixation; the latter, achieved by casts followed by suitable braces, should be continued until skeletal maturity or until a tibia of relatively normal size develops. In patients with extreme deformity, amputation may be indicated when one is reasonably sure that a prosthesis will provide a better weight-bearing extremity than the best extremity that could be obtained after successful reconstructive surgery. In making the decision, the surgeon should compare the function of an artificial leg with the best result that can reasonably be expected after reconstructive surgery, not with a normal extremity. Repeated clinical and roentgenologic examinations should be continued until skeletal maturity is reached. If at any time evidence of narrowing of the bone or sclerosis of the medullary cavity appears, prophylactic operative intervention with wide resection of the constricting band of scar tissue should be done. In addition, reinforcing grafts should be placed about the area of previous pseudarthrosis. Multiple operations may be necessary during the growth period. A registry for congenital pseudarthrosis of the tibia is needed in order to enhance knowledge of the causation, pathology, treatment, and end-results through the age of skeletal maturity.

Significance of Mineral Metabolism in Surgery. E. Carstensen. Chirurg **29**:536-541 (Dec.) 1958 (In German) [Berlin].

The author studied the metabolism of water and minerals in 80 patients who underwent operations of moderate or extensive type at the surgical clinic of the University of Hamburg–Eppendorf, Germany; these included such surgical interventions as gastrectomy, cholecystectomy, amputation of the rectum, pulmonary resection, strumectomy, and radical removal of mammary glands. The studies of metabolism were carried out preoperatively and postoperatively. In the course of and after the surgical intervention, the patients were given infusions of dextrose and fructose without the addi-

tion of minerals. Rarely the amount of transfused citrated blood exceeded 250 to 500 cc. The variations in electrolytes in the serum and the urine were markedly uniform, independently of the extensiveness of the surgical intervention, provided that no complications occurred in the field of the operation. After increased elimination of potassium on the first and the second postoperative day, the potassium reached its lowest value in the serum on the 3rd or the 4th postoperative day. On the 6th or the 7th postoperative day, the serum potassium level and the potassium elimination became normal again. It seems likely that the increased postoperative potassium elimination by the kidneys and the resultant relative hypopotassemia may be a sequela of the stimulation of the adrenal cortex by the "operative stress." Postoperative determination of the cortisone serum level revealed that it was considerably increased and that the highest value was reached 6 hours after the operation. On the 5th postoperative day the cortisone serum level was restored to normal. The postoperative hypopotassemia seldom reached values of less than 4 mEq. in the serum. The term "compensated hypopotassemia" is suggested because of the absence of clinical symptoms and since the condition does not require any therapeutic measures.

Decompensation of the electrolyte and particularly of the potassium metabolism threatens only after postoperative complications, such as peritonitis, ileus, major suppuration, and intestinal fistulas. Prolonged postoperative feeling of thirst for more than 2 or 3 days, or increasing thirst, is suggestive of the onset of such complications. Increased loss of potassium may be manifested by feeling of weakness, hypotonia of the skeletal muscles, cyanosis of pulmonary origin, atonia of smooth muscles, nausea, and vomiting. The organism then is no longer able to compensate spontaneously for the potassium loss, and administration of infusion solutions containing electrolytes and carbohydrates becomes indispensable. The electrolyte losses of patients with an uneventful postoperative course are clinically insignificant, and electrolyte substitution therapy is not necessary. An exaggerated infusion activity may even be more harmful than useful. Therapeutic electrolyte infusions with flame-photometric control are required in patients with postoperative complications occurring in the operative field.

Potassium Metabolism and Potassium Substitution Therapy in Patients Subjected to Surgical Interventions. G. M. Dummer. Chirurg 29:541-544 (Dec.) 1958 (In German) [Berlin].

In the course of surgical intervention and in the postoperative phase, potassium exerts a particular influence on the biological behavior, i. e., on the composition and distribution of electrolyte solutions in the 3 body spaces of the patient, namely, the cell, the interstice, and the intravascular space. Every normal operative intervention is associated with a loss of potassium. Intracellular acidosis with alkalosis of the extracellular fluid results from a change in hydrogen ions. In the absence of postoperative complications the organism is able to compensate for the alkalosis of the extracellular fluid, but the acidosis in the cells may be compensated for only when the organism has taken up again adequate amounts of potassium and monosaccharides and a normal glycogenesis has been reestablished.

The symptoms of potassium deficiency, i. e., a serum potassium level of less than 13 mg. per 100 cc. (3.3 mEq. per liter), may vary from general weakness to flaccid paralysis of the extremities with abolition of tendon reflexes; they have often prevented an operation from being successful. The request, therefore, is advanced to provide for potassium substitution before, in the course of, and after the surgical intervention. Substitution by mouth represents the most favorable method. Fruits, vegetables, meat, milk, and their derivatives are rich in potassium, but it is difficult to compute a diet with an excess in potassium while commercial potassium salts can be added easily to the diet. Oral administration of potassium, however, is rarely feasible in surgical patients, and, therefore, infusion treatment is the method of choice.

Two groups of surgical patients must be distinguished as follows. The first group consists of those without significant preoperative or postoperative potassium loss, and the second group consists of those with a preoperative potassium deficiency or those in whom a major postoperative loss of potassium is caused by the necessary removal of gastric juice and intestinal juice respectively. The solution used for patients in the first group should contain 2 Gm. of potassium chloride per liter, corresponding to about 1 Gm. of potassium. It should also contain sodium chloride. Up to 1,500 cc. of such a solution was used by the author with highly satisfactory results on the day of the operation, and amounts of 500 to 1,000 cc. were given on the following days according to need. The pH value of 7.2 of this solution corresponded with the blood pH. The addition to the solution of 25 Gm. of dextrose and 25 Gm. of fructose accelerated the transport of potassium into the cell body. In patients with severe hypopotassemia, an adequate amount of sterile 10% potassium chloride solution and dextrose was added to the infusion solution. The use of a flame photometer for serum potassium and sodium determinations is strongly advocated.

NEUROLOGY & PSYCHIATRY

Leucotomy for Pain. A. Elithorn, E. Glithero and E. Slater. J. Neurol. Neurosurg. & Psychiat. **21**:249-261 (Nov.) 1958 [London].

The authors report on 13 men and 12 women, between the ages of 31 and 78 years, who underwent operations of leukotomy type for the relief of intractable pain and were followed up for periods ranging from 17 to 78 months, with an average of 40 months. Nine patients had "extensive" operations, consisting of full bilateral "standard" operation in 7 and full unilateral operation with partial incision on the contralateral side in 2. Three patients had only a unilateral standard leukotomy, and 13 patients had "limited" operations in which half or less of the white matter of the frontal lobes was divided. The results of the operations were assessed by the patient and by the relative most concerned, clinically; they also were assessed with a rating scale, including symptoms, employment, family relationships, and community relationships, thus still depending on the subjective evaluation of quantitative data but, nevertheless, permitting a more detailed assessment of the efficacy of the treatment.

Clinical evaluation suggested that 17 of the 25 patients had been clearly helped by the operation. Twenty (80%) showed an over-all gain on the social rating. However, only 8 (35%) of 23 patients and 8 (38%) of 21 relatives thought that the operation had been worthwhile. The tendency for patients and relatives to be dissatisfied with a leukotomy for intractable pain was related to the observation that, although most patients admitted to some improvement in their symptoms, only 5 thought that their pains were less intense. With regard to the type of operation performed, the patients and relatives all agreed and the clinical assessment showed that more favorable results were obtained from "extensive" operations than from "limited" ones. In contrast, patients who had "limited" operations tended to show bigger gains on the social rating scale. This discrepancy is related to the fact that, while more, extensive operations tend to produce greater relief from suffering, they also are more likely to lead to socially crippling defects of personality.

The results obtained support the following conclusions. Operations on the frontal lobes—unless they are very extensive—do not impair the patient's ability to perceive and react appropriately to a painful stimulus, but they produce relief by impairing his ability to elaborate a persisting attitude or mood. The probability that leukotomy will provide relief for a patient with intractable pain depends, first, on the severity of the painful sensations and, secondly, on the nature of the psychological reaction. In patients in whom the pain is not severe and the psychological reaction is largely a depressive or anxious preoccupation with symptoms, the prospects of some degree of relief are high. If pain is severe and frequent, little permanent relief is to be expected. In patients with hysterical tendencies, these may be increased, but, since the anxiety which provokes the hysterical symptoms may be reduced, the total change is often a gain in social adaptation. Operations on the frontal lobe are an unsatisfactory treatment for intractable pain, but, if pain cannot be alleviated by other means, then in carefully selected patients operations of leukotomy type may produce both relief from suffering and an improved social adjustment.

A Controlled Study of the Effects of Leucotomy. A. A. Robin. J. Neurol. Neurosurg. & Psychiat. **21**:262-269 (Nov.) 1958 [London].

The author compared the results in 155 women and 43 men treated by leukotomy at Runwell Hospital in Wickford, Essex, England, with those in 198 control patients matched for chronicity (length of stay in hospital), age on admission, sex, and being treated at the same time. Leukotomy did not appear to (1) improve the chances of discharge from the hospital, (2) accelerate discharge, (3) reduce the chances of readmission, (4) delay readmission, (5) reduce the number of readmissions, (6) reduce the total period of readmission, (7) improve hospital behavior as judged by ward level, and (8) significantly increase the death rate. A second leukotomy did not significantly improve the patients' prospects of discharge in relation to the controls. The sex of the patients did not influence the results of leukotomy. "Recovered" patients, i. e., patients who have been discharged from hospital and have not since been readmitted to Runwell or any other mental hospital in England and Wales under the same name, had at least the same level of adjustment in the control group as in the group subjected to leukotomy, and they seemed similar in that they showed the same distribution of diagnoses, ages, and lengths of stay in hospital. No evidence was found for a delayed operative response after leukotomy.

GYNECOLOGY & OBSTETRICS

The Transmission of Transfused Sickle-Trait Cells from Mother to Fetus. N. T. Macris, L. M. Hellman and R. J. Watson. Am. J. Obst. & Gynec. **76**:1214-1218 (Dec.) 1958 [St. Louis].

This paper describes a method by which it is ascertained whether intact maternal erythrocytes cross the placental barrier. Donor blood with the sickle-cell trait but without sickle-cell anemia was selected for this purpose. When erythrocytes with the sickle trait are exposed to a decreased oxygen

tension, they assume a characteristic sickled configuration which is easily recognized. A group of pregnant women was, therefore, injected with sickle-trait blood, and the blood of their infants was examined for sickle cells. The subjects of this study were 25 Rh-positive pregnant women at or near term. Specimens of their blood were examined for sickle cells, and in all except one none were found. When available, the husband's blood was also examined for sickling. The selection of subjects in this study was governed largely by the blood group of the sickle-trait donor blood that was available. They ranged in age from 17 to 38 years and included 18 Negroes, 4 Puerto Ricans, and 3 whites.

Twenty-one of the subjects were transfused with 500 ml. each of sickle-trait whole blood. In 3 instances the supernatant plasma in 500 ml. of whole blood was removed, allowing the sickle-trait cells to be given in a reduced volume. The elapsed time, between the end of transfusion and delivery, ranged from 40 minutes to 153 hours and 2 minutes. Nineteen of the women were delivered vaginally, and 6 by cesarean section. Whole blood was collected both from the umbilical cord at delivery and from the mother within 12 hours after delivery. Sickle-cell preparations of the mother's and infant's bloods were prepared.

Sickle cells were found in the umbilical cord blood of the newborn infant in 3 of the 25 cases studied. The placenta in each of the 3 cases was normal on gross inspection. The placental passage of sickle-trait cells in 3 of 25 experimental subjects adds to the already existing evidence that in a small percentage of patients maternal red blood cells traverse the placental barrier and are found in appreciable numbers in the fetal circulation. The mechanism of transfer is obscure. While breaks are known to occur in the fetal circulation, the pressure relationships are thought to be such that direct passage must always occur from fetus to mother. Direct transfer of maternal cells against the pressure gradient is not feasible. Furthermore, the venous pressure cannot fall below the amniotic fluid pressure, which is the same as the intervillous space pressure. The only remaining possibility is active transfer by the process of planocytosis, which has been shown to occur for particulate matter. When certain rough assumptions were made from the data, the fetus in at least one instance must have received at least 5 ml. of sickle-trait cells. Should the placenta be unable to distinguish between sickle-trait and normal maternal cells, the transfusion to accomplish this must have been a bit more than 40 ml., which is altogether unlikely. One is left with the assumption that the microvilli distinguish between natural and unnatural maternal cells, engulfing only the latter. The facts of transfer can no longer be denied. The mechanism remains a baffling mystery.

The Nasal Mucus Smear in Toxemias of Pregnancy. E. H. Abou-Shabanah, J. G. Boutselis, W. J. Frajola and J. C. Ullery. Am. J. Obst. & Gynec. **76**:1248-1263 (Dec.) 1958 [St. Louis].

Observations indicate that among pregnant women who are apparently normal during early pregnancy there are some who are potentially preeclamptic, and that significantly greater weight gain occurs in the patient with preeclampsia between the 13th and 20th weeks of pregnancy than in the normal or hypertensive pregnant patient. Eclampsia has been known to occur sometimes without the development of proteinuria or hypertension. Although edema is one of the principal signs of the preeclamptic state, it is possible for true preeclampsia to occur with no pitting edema and with only excessive weight gain. This weight gain is usually too rapid to be accounted for by the growth of the fetus or the gravid uterus. Perhaps an intracellular accumulation of fluid occurs in preeclampsia. Healthy pregnant women also have delayed water excretion and some sodium chloride retention, presumably because of increased activity of the adrenal cortical hormones. In the past storage of water and sodium chloride without obvious edema was difficult to understand. Today, with evidence in favor of the ability of sodium to replace intracellular potassium, the latter being excreted, occult edema can be explained. In other words, one expects sometime during the course of preeclampsia–eclampsia to find a change in the ratio between sodium and potassium excreted in body fluids. The study of potassium excretion in the urine revealed no characteristic curve for preeclampsia. In this paper the authors demonstrate the value of the nasal mucous smear in the study of the toxemias of pregnancy.

In a preliminary study, nasal mucous smears were made on 5 patients at the Demerdash Hospital, Cairo University, Egypt—3 in the preeclamptic phase and 2 in eclamptic convulsions. The excretion of sodium and potassium in the nasal and cervical mucus of normal pregnant women was studied in an attempt to relate the sodium and potassium excretion to the fern phenomenon. Some of the mucus, as obtained, was spread on a slide for the fern test, while the remainder was treated with a minimum of dilute hydrochloric acid and water, filtered to remove strands, and the filtrate analyzed for sodium and potassium content by flame spectrophotometry. The nasal mucus from 30 pregnant women, who on admission presented signs and symptoms of late toxemia of pregnancy, was examined. Nasal smears were taken on admission, then hourly in severe cases, and twice daily in others.

Nasal mucous smears were classified on the basis of the presence or absence of arborizations. When arborizations were present, a further classification was made according to whether the pattern showed

beaded arborizations (unlinked arborizing crystals) or an atypical fern (deficient or incomplete fern arborization). Oils of different refractive indexes were used to identify the presence of calcium or potassium on the smear. The absence of arborization (negative fern phenomenon) in a smear of nasal mucus is associated with preeclampsia–eclampsia. The sodium-potassium ratio of the nasal mucus of normal pregnant women and of pregnant women with hypertension and/or renovascular disease is greater than 1, whereas in preeclampsia–eclampsia it is reversed. The use of index of refraction oils on smears of nasal mucus will enable the physician to detect preeclampsia by a simple office test. This test also guides him in the management of, and the prognosis for, both mother and fetus.

Management of the Pregnant Diabetic. W. S. Jones. Diabetes **7**:439-445 (Nov.-Dec.) 1958 [New York].

Among the 140,665 deliveries at the Providence (R. I.) Lying-in-Hospital in the 31-year period from 1927 to 1957, there were 273 pregnancies in 169 diabetic women. After excluding abortions and dubious diagnoses, there remained 251 viable pregnancies, on which this study is based. The prevalence of prepaid insurance coverage has created a progressive shift from clinic to private patient status. The 93 private deliveries were conducted by 26 different obstetricians, and 43 internists and general practitioners participated in their medical management. This lack of uniformity of control is in marked contrast to that in a teaching hospital. Furthermore, many patients resist long periods of hospitalization desirable in the last trimester, and the community obstetric service is obliged to accept emergency cases and miscellaneous drifters, infrequently seen in specialized centers. This has a devastating effect on fetal loss statistics.

Answers were sought to two questions: What kind of diabetic women lose their babies, and under what circumstances? Fetal loss was investigated in relation to the age of the mother, the age at which she acquired diabetes, and the duration and severity of her diabetes. The great majority of fetal deaths was associated with 3 clinically detectable physiological complications: 1. In the presence of acidosis, the fetal loss was 51%. 2. In women with preeclampsia, 32% of the infants died. 3. In cases in which hydramnios was recorded, the wastage was 37%.

The author feels that progress in improving fetal salvage in diabetes seems painfully slow. The loss over a 31-year span was 28%, and it has remained close to 25% in recent periods. Much of this loss occurs among older women and among those with mild forms of diabetes—patients in whom better results should be achieved. Much of the fetal loss stems from small but costly slips in diabetic control and from debatable obstetric judgment. The author believes that improved fetal salvage will come about, not by emptying the uterus earlier or by doing more cesarean operations, but by paying closer attention to the control of diabetes and toxemia.

Diverticulitis, Sigmoiditis and Perisigmoiditis from Gynecologic Viewpoint. J. A. Abolins. Nord. med. **60**:1568-1569 (Oct. 30) 1958 (in Swedish) [Stockholm].

Diverticulitis can cause both diagnostic and therapeutic difficulties. The disease seems to occur more frequently. When a resistance in the small pelvis is found, especially with inflammation, the possibility of diverticulitis, sigmoiditis, or perisigmoiditis should be considered. The history gives valuable information. Usually for a long time before the first consultation there has been constipation, diarrhea, and flatulence. The commonest symptom is abdominal pain on the left side, together with fever. Roentgenologic examination is desirable, but in the acute stage it is not without danger. Often the first roentgenologic examination does not give certain diagnosis. Conservative treatment is advised. The 6 cases of diverticulitis described were observed during a half-year period in patients admitted on the diagnosis of gynecologic disease. Diverticulitis was established at laparotomy or on roentgenologic examination. Treatment was with antibiotics, salazopyrine, and diet. The patients continue free from symptoms after 2 years.

Fetomaternal Leukocyte Incompatibility. R. Payne and M. R. Rolfs. J. Clin. Invest. **37**:1756-1763 (Dec.) 1958 [New York].

Isoleukoagglutinins are known to develop primarily in patients who have received many transfusions, but there may also be other stimuli for leukoagglutinin production. Investigators have drawn upon the analogy to Rh antibody formation and have discussed the possibility that fetal leukocyte antigens might act as stimuli to the mother. The studies presented in this paper demonstrate that fetomaternal leukocyte incompatibility may induce leukoagglutinin formation in the mother and suggest that some leukocyte factors, as demonstrated by their corresponding leukoagglutinins, may be genetically transmitted to the offspring. Serums were collected from 3 groups of women. Group 1 included 144 obstetric clinic patients selected with the sole qualification of multiparity; all women had had 4 or more pregnancies. The majority of the women were in the third trimester of pregnancy, while a few were in the second trimester, as it was thought that more easily detectable amounts of antibody might be present in parous women during late pregnancy. Group 2 consisted of 8 patients who were included because

they showed varied circumstances in which leukoagglutinins could be found in parous women. The majority of group 2 had Rh antibodies. There was A-O incompatibility between newborn infant and mother in one instance; another patient was referred because of an anemia of unknown origin; and the last had had a febrile transfusion reaction. Group 3, a control series, consisted of 20 healthy women who had never been pregnant and had never received transfusions.

Leukoagglutinins were found in 25 (or 17%) of the 144 multiparous women. They were completely absent in the controls who had never been transfused or been pregnant. The fetus appeared to be the only stimulus for leukoagglutinin production in 18 of the 25 women, since this number had never received transfusions or blood injections. Isoleukoagglutinins of the maternal serums agglutinated the leukocytes of 10 of 12 of the patients' respective newborn infants, and 12 of 13 of their respective spouses, thus suggesting the inheritance by the offspring of the fathers' leukocyte factor. Maternal sensitization to leukocytes appears to develop in a manner analagous to Rh sensitization.

PEDIATRICS

Streptococcal Infection in a School Population: Preliminary Report. D. Cornfeld, G. Werner, R. Weaver and others. Ann. Int. Med. **49**:1305-1319 (Dec.) 1958 [Lancaster, Pa.].

Evidence that prompt and continued treatment of streptococcic infections of the throat may greatly reduce the incidence of primary attacks of rheumatic fever has been obtained largely from military establishments, in which groups are at the risk of epidemic transmission of infectious disease, and in which infection may be subjected to epidemiologic studies. The studies presented here aimed to ascertain whether children of school age, the group most vulnerable to rheumatic fever, can be protected from first attacks of rheumatic fever in a manner similar to that found to be effective in military groups. Three schools in south Philadelphia were selected to furnish for study a population of approximately 1,000 children. During the school year, clinical epidemiologic and bacteriological data were obtained from the children and, where indicated from their family contacts. The aim was to determine: (1) the carrier rate of beta-hemolytic streptococci, (2) the rate of clinically manifest streptococcic infection, and (3) the effect of various treatment programs on both the carrier rate and the rate of clinically manifest infection.

In each of the school years, approximately one-half of the children had one or more positive cultures for beta-hemolytic streptococci, regardless of attempts to control carriers by penicillin treatment. The rate of clinically manifest streptococcic infection remained relatively low in all schools, independent of the existing carrier rate or treatment programs instituted. Relatively few of the children with respiratory symptoms had positive cultures for beta-hemolytic streptococci, and even in the group with positive cultures most of the children presented symptoms of undifferentiated respiratory tract illness. Most of the beta-hemolytic streptococci isolated were of group A, but a large percentage of these could not be typed. The poured-plate method of growing streptococci permitted a significantly higher recovery rate than did any enrichment method or direct streaking method tried. In view of the data presented, the authors question the efficacy of the currently popular programs based upon bacteriological culture studies on school children and penicillin treatment for those found to harbor streptococci in their throats.

Spontaneous Perforation of Bile Ducts in Infancy. T. C. Gertz. Ugesk. læger **120**:1454-1458 (Oct. 30) 1958 (In Danish) [Copenhagen].

Spontaneous perforation of the bile ducts in infancy is a rare disorder. The first 2 cases of the entity were described by Caulfield in 1936; 8 additional cases have since been published. Spontaneous perforation of the bile ducts in infancy is characterized by mild intermittent jaundice, acholic stools, absence of bile pigment in the urine, gradually increasing distention of the abdomen with ascites, and often bilateral inguinal hernias containing fluid. The case which the author describes in a female infant, aged 4½ months, recently treated in the Rigshospitalet, Copenhagen, is the 11th case to be reported. The spontaneous perforation of the choledochus in this patient probably originated at the age of 5 to 9 weeks. Cholecystocholangiography revealed a perforation in the choledochus. On operation large amounts of bile-colored ascites fluid were found from an abscess under the right liver lobe. The postoperative course after simple drainage of the choledochus was uneventful, and the patient was discharged as well a month later. The disease is usually subacute but can sometimes be acute. In untreated patients it is fatal. It is important to know the disease so that diagnosis can be timely. Operation with simple drainage of the choledochus region has proved curative in most cases. Preoperative cholangiography is a valuable diagnostic aid.

The Development of Prematurely Born Children with Birth Weights or Minimal Postnatal Weights of 1,000 Grams or Less. M. Dann, S. Z. Levine and E. V. New. Pediatrics **22**:1037-1053 (Dec.) 1958 [Springfield, Ill.].

The authors report observations on the physical, mental, and social development of 73 children with very low birth weights, born prematurely between

Jan. 1, 1940, and Dec. 31, 1952, who were discharged alive from the premature nursery of the New York Hospital and were examined between October, 1950, and November, 1957. Of the 73 children, 37 were in the statistical birth weight group of from 660 to 999 Gm. (1½ to 2¼ lb.) and 36 weighed 1,000 to 1,280 Gm. (2¼ to 2¾ lb.) at birth, but their weight fell to 1,000 Gm. or less in the neonatal period. At the time of the examination, 32 children had reached the age of at least 4 years, and the oldest child was 10 years old. In 34 families in which there was a full-term brother or sister, 4 years of age or older, these siblings served for comparison. For obvious reasons, these full-term children were not strictly comparable with the premature group, but they had the same parents and essentially the same home environment.

With rare exceptions, physical health of the prematurely born children was good, with a marked paucity of neurological defects. They showed a tendency to catch up in height to normal standards for chronological age, but often not until after 4 years of age. The incidence of eye defects, especially strabismus and myopia, was high. Intelligence quotients showed a wide range from 59 to 142; the average intelligence quotient was 94, and it was significantly below that of 107 found in the 34 full-time siblings examined for comparison. Twelve of the 73 prematurely born children had intelligence quotients below 80; among the 43 of similar birth weight but not available for examination, 19 were known to be mentally retarded, and 5 of these were in institutions. A significantly higher proportion of the children with intelligence quotients above 100 was found among families of higher socioeconomic rating. A suggestive advantage of girls over boys and of white over nonwhite children was noted, though the latter factor was probably secondary to socioeconomic factors. A high incidence of serious maternal complications existed and might well have influenced the outcome, but within the group no relationship was found between lower intelligence quotient and complications of pregnancy and delivery, with the possible exception of toxemia and cesarean section. There was no greater incidence of low intelligence quotient in patients with visual handicaps than in the total group.

An Additional Contribution to the Study of Constitutional Methemoglobin Cyanosis: Description of Two Cases. G. Bono and P. C. Gamalero. Minerva pediat. **10**:1076-1082 (Oct. 13) 1958 (In Italian) [Turin, Italy].

The authors report on 2 male children, brothers, 6 and 3 years old, respectively, with cyanosis. Abnormal amounts of methemoglobin were found in the blood of both patients. The condition was manifest on the skin and on the mucous membranes and became marked on fatigue or when the children cried. The first child also presented clubbed fingers, tracheobronchial adenopathy of tuberculous nature, and latent dyspnea; mild dysrhythmia with slow diffused waves was noticed on electroencephalographic examination. Marked erythrocyte fragility was present in both children and in their parents. The patients were treated with large doses of vitamin C given cyclically by intravenous injection and by mouth for prolonged periods of time.

DERMATOLOGY

Treatment of Persistent Acne in Women with 17 Alpha Hydroxyprogesterone Caproate (Delalutin): A Preliminary Report. K. C. Baker. J. Invest. Dermat. **31**:247-250 (Nov.) 1958 [Baltimore].

Seventy-six women, between the ages of 15 and 36 years, with acne, 69 of whom had a definite history of premenstrual exacerbation of the eruption, were treated with 17-alpha-hydroxyprogesterone caproate (Delalutin), an esterified derivative of the naturally occurring progestational hormone. The group included patients with 4 different clinical types of acne; a diagnosis of acne vulgaris was made in 37 women, of acne cystica in 19, of acne rosacea in 3, and of acne sebacea in 17 patients. A single dose of 125 mg. (1 cc.) of this long-acting drug was injected deeply into the gluteal muscle between the 14th and the 18th day after the onset of menstrual flow. Injections were given for a total of 2 to 8 months during the course of the study. Standard therapeutic measures in current use had failed to control the manifestations of acne in these patients. A good to excellent response, as indicated by the clearing of existing lesions and by the prevention of new lesions, was achieved as a result of treatment with this progestational agent in 64 of the 76 patients. A single injection of the steroid ester given once a month and repeated 2 to 6 times thus considerably improved the appearance of the skin. In the dosage administered, hydroxyprogesterone caproate was well tolerated. An alteration in the menstrual pattern (with scanty menses) was observed in one patient during the course of therapy. When the hormone injections were discontinued, however, the menstrual flow again assumed its usual characteristics.

The prolonged effect of the progestogenic compound (10 to 14 days) is thought to resemble the sustained action of the continuous endogenous production of progesterone by the corpus luteum. In comparison, free progesterone has a relatively brief effect (2 to 3 days). The availability of hydroxyprogesterone caproate with a prolonged progestational activity makes possible a physician-controlled regimen which maintains a high progesterone level in rhythm with the normal menstrual cycle. The

reported data suggest that hydroxyprogesterone caproate should be given an extensive trial either alone or in conjunction with other systemic and local measures as a therapeutic agent in women with persistent acne.

A Localized Outbreak in New York of Tinea Capitis Due to Trichophyton Violaceum: Observations with Special Reference to Mixed Infections of the Scalp. S. A. Rosenthal, D. Fisher and D. Furnari. A. M. A. Arch. Dermat. **78:**689-691 (Dec.) 1958 [Chicago].

Infection of the scalp with Trichophyton violaceum is a rare finding in the United States, although it is common in other areas of the world. The observation of 2 species of fungi simultaneously infecting the same scalp is likewise rare. This paper reports on a localized outbreak of tinea capitis due to T. violaceum, with observations on mixed fungous infections of the scalp, in the Willowbrook State School, Staten Island, N. Y. (for mentally retarded persons). T. violaceum was isolated from 44 of 88 subjects with clinical tinea capitis. A surprisingly large number of mixed fungous infections of the scalp was observed. Of 71 subjects with culturally proved tinea capitis, 33 (46%) showed a mixed scalp infection, with 4 of these each yielding 3 species of fungi.

The clinical picture seen in this series of scalp infections with T. violaceum did not usually show the classic, "black dot" type of morphology. Infected areas showed various degrees of scaling and erythema with broken-off hairs several millimeters long. Often normal-appearing hairs were also present in these areas. The source of the T. violaceum outbreak in this state school is unknown. The close personal contact necessitated by institutional life may well be a cause of considerable dissemination of fungous diseases due to species which otherwise rarely produce disease in the United States.

Skin Lesions Caused by Chlorpromazine. W. G. van Ketel, J. J. Morriën and H. H. Lenstra. Nederl. tijdschr. geneesk. **102:**1799-1804 (Sept. 13) 1958 (In Dutch) [Amsterdam].

Published reports show that chlorpromazine sometimes produces skin lesions of the cutaneous vascular type, particularly in patients treated with large doses. The epidermis shows no pathological changes, and the skin lesions rapidly disappear after chlorpromazine therapy is discontinued. After recovery it is often possible to resume treatment with chlorpromazine in smaller doses. It has also been pointed out that it is not always necessary to stop the administration of chlorpromazine, for the skin eruption may subside if the dose is only reduced, or even if it is not changed at all. Tests have revealed that exposure to sunlight may intensify eruptions brought on by chlorpromazine.

Cutaneous lesions that result from sensitization to chlorpromazine by external contact present a different problem than the eruptions caused by medication. An allergic contact dermatitis localized chiefly on the fingers and around the eyes may develop in nursing personnel handling tablets or solutions of chlorpromazine. The authors found that 7 of 62 members of the nursing staff in a small hospital had contact dermatitis; in 5 of these patients the dermatitis was due to chlorpromazine, in 1 chiefly to streptomycin, and in 1 to penicillin. The patch test is valuable in the diagnosis of contact eczema. The onset of the contact dermatitis is usually more delayed, but its prognosis is less favorable than that of the eruption resulting from treatment. No general statement can be made with regard to the influence of exposure to sunlight on the contact dermatitis. Although in one patient such exposure caused an exacerbation, in others the lesions developed in winter, and patch tests combined with sun exposure or ultraviolet irradiation could not be carried out. Repetition of sensitivity tests showed a lessening of sensitivity in some of the patients. A study was made of the most suitable concentrations for testing sensitivity reactions. Cross sensitivity for chemically related preparations, notably promazine, could not be established.

THERAPEUTICS

A Study of the Effectiveness of Certain Anorexigenic Agents. J. F. Fazekas, W. R. Ehrmantraut and J. Kleh. Am. J. M. Sc. **235:**692-699 (Dec.) 1958 [Philadelphia].

The authors conducted double-blind studies of the anorexigenic effects of phenmetrazine hydrochloride, a combined preparation of dextro amphetamine sulfate and amobarbital, and a placebo. Phenmetrazine hydrochloride and a placebo were given to, and their effects compared in, a group of 106 obese, mentally normal persons, and, in order to obviate insofar as possible the influence of suggestion, all 3 agents were given to, and their effects compared in, a group of 43 obese, mentally deficient persons. The study was terminated after 28 weeks. In both the mentally alert and the mentally deficient persons, there was a significant reduction of weight with phenmetrazine but no significant change during the placebo administration. Subjective undesirable side-effects, which were evaluated only among the mentally normal persons, disclosed no apparent difference between phenmetrazine and the placebo. In the mentally deficient group, the weight loss induced by dextro amphetamine sulfate was similar to that obtained with phenmetrazine. It is postulated that these drugs act primarily in subcortical areas, probably by influencing localized neurohumoral activity. In view of the almost cer-

tain influence of the cortex and spinal cord, as well as the subcortex, on appetite, it should not be surprising that there is considerable variability in individual response to anorexigenic agents.

The Clinical Investigation of a Codeine Resin Complex: A Long Acting Analgesic for Oral Administration. L. J. Cass and W. S. Frederick. New England J. Med. **259**:1108-1111 (Dec. 4) 1958 [Boston].

The search for an improved analgesic that can provide effective and sustained relief of pain without appreciable side-effects prompted this study. Experiments in animals have shown that the toxicity of codeine is substantially reduced when it is administered as an ion-exchange resin complex, and also that the analgesic action of the resin complex is potentiated by the addition of certain amines that in themselves have little or no pain-suppressing activity. It seemed desirable to undertake an evaluation of several formulations of the codeine resin complex with other compounds and compare them with a standard preparation, such as mixtures of codeine and acetylsalicylic acid, phenacetin and caffeine citrate.

Eleven analgesics were evaluated in 3 separate clinical experiments on 65 patients with various painful conditions, their ages ranging from 40 to 60 years. Data obtained from a total of 24,640 observations showed that the codeine-methyl-orthotolyl-quinazolone resin complex is an effective, long-acting analgesic, in which the synergistic action of the quinazolone derivative makes it possible to reduce the daily total dosage of codeine required to control moderate pain. It was demonstrated that this drug has a greater pain-suppressing effect—for 12 hours after a single dose—than standard codeine combined with acetophenetidin, aspirin, and caffeine.

Experimental and Clinical Research on the Action of Soybean Oil on Cholesterolemia. R. Wolff, R. Herbeuval, G. Cuny and others. Presse méd. **66**: 1706-1708 (Nov. 1) 1958 (In French) [Paris].

Alimentary lipids play a large part in the regulation of cholesterolemia. Recent studies have distinguished the action of fats of vegetable origin from that of fats of animal origin. The suppression of animal fats and generally fats rich in saturated fatty acids lowers the level of blood cholesterol. Vegetable oils introduced into the diet in about 40 to 50% of caloric needs exert a hypocholesterolemic action. This action is related to the richness of the fats in unsaturated fatty acids. It is not as yet agreed as to the nature of the unsaturated fatty acids responsible for lowering the cholesterol level. The unsaturation of oils is due to the presence of fatty acids in one or several combinations. These combinations are measured by the iodine index. It was found that the iodine index of soybean oil is high (higher than that of corn oil). Soybean oil contains 4% of vegetable sterols of the beta-sitosterol type. This sterol exerts a hypocholesterolemic action in rabbits and in man by checking the intestinal absorption of cholesterol of exogenous origin. A priori, soybean oil is susceptible of having a hypocholesterolemic action by its degree of unsaturation and by its richness in beta-sitosterol.

The action of soybean oil from the experimental and clinical viewpoints was studied in the laboratory of biological chemistry and in the clinic for diseases of older patients at the Medical School of Nancy. Five lots of 6 to 8 rabbits were given a special feeding with 3 ml. of soybean oil per kilogram of body weight for a period not exceeding 8 days. After this administration there was noted a drop in the level of blood cholesterol, which reached 23 to 31% of the initial value and occurred as early as the next day. Research on man was carried out by studying 15 men whose ages ranged from 50 to 70 years. All except 2 had different manifestations of arteriosclerosis. Nine had arteriosclerotic fundus oculi, with lesions of the capillaries in the retina and cholesterol deposits. Six had arterial hypertension. At the beginning the level of blood cholesterol was high in all subjects—from 2.42 to 4.50 Gm. They were put on a diet with the administration of 1.5 cc. of soybean oil before each of the 2 main meals. In 6 subjects for whom the diet was of short duration (6 to 11 days), a constant fall in the level of total cholesterol was noted. The average fall was to 16% of the initial value. In 9 subjects the administration of soybean oil was of long duration (an average of 63 days). The findings regarding cholesterol level in this group were heterogeneous and difficult to interpret. Despite the presence of large amounts of unsaturated fatty acids of the "essential" type in soybean oil, the action of this oil on cholesterolemia is questionable. Factors other than the unsaturation of fats must intervene in the regulation of blood cholesterol.

An Inter-Relationship Between Ascorbic Acid and Cyanocobalamin. E. V. Cox, R. Gaddie, D. Matthews and others. Clin. Sc. **17**:681-692 (Nov.) 1958 [London].

Deficiency of cyanocobalamin, vitamin B_{12}, is closely associated with megaloblastic anemia, and a deficiency of ascorbic acid gives rise to scurvy. The authors cite previously reported observations that suggest an association between these two vitamins, but as yet definite evidence of this in an adequate number of patients is lacking. The investigations reported in this paper were undertaken to determine whether there was indeed any relationship between B_{12} and ascorbic acid. The effect of B_{12} administration on the plasma concentrations of ascorbic acid before and after an intravenous injec-

tion of 250 mg. of sodium ascorbate was studied in patients with pernicious anemia, in adults with celiac disease, and in patients with regional ileitis. The patients with low serum B_{12} levels had significantly lower plasma ascorbic acid levels than normal controls.

The rate of disappearance of the injected sodium ascorbate was increased in the state of vitamin B_{12} deficiency—in patients with pernicious anemia, 38.7%; in adults with celiac disease, 39.3%; and in patients with regional ileitis, 36.0%—compared with 24.4% in healthy subjects. After B_{12} therapy the abnormal ascorbic acid metabolism was corrected in patients with pernicious anemia and improved in adults with celiac disease. No change was noted in those with regional ileitis. The effect in pernicious anemia and in celiac disease of adults was masked in those partaking of diets containing a plentiful or a grossly deficient supply of ascorbic acid. In regional ileitis, the lack of effect of B_{12} was attributed to the activity of the underlying disease; a significant correlation was noted between the levels of seromucoids and plasma ascorbic acid. The effect of B_{12} deficiency on ascorbic acid metabolism was greater when the deficiency was associated with a megaloblastic anemia in patients with pernicious anemia and celiac disease of adults than it was in similar patients with a normal erythropoiesis.

Folic Acid and Cyanocobalamin in Pernicious Anaemia. E. V. Cox, M. J. Meynell, W. T. Cooke and R. Gaddie. Clin. Sc. **17**:693-699 (Nov.) 1958 [London].

The observation that vitamin B_{12} deficiency can occur without megaloblastic anemia has been noted repeatedly, and it is difficult to explain the hematopoietic defect of pernicious anemia solely on the basis of B_{12} deficiency. A deficiency of folic acid would appear to be of little therapeutic significance, since supplementary folic acid is rarely required in pernicious anemia. The therapeutic activity of folic acid and the lack of anemia in some patients with B_{12} deficiency, however, indicate the possibility of a relationship between these compounds. In this study the authors investigate the metabolism of folic acid in pernicious anemia and observe the effect of B_{12} therapy. Folic acid (5 mg.) was given intramuscularly to 20 normal subjects, 23 hospital patients with no evidence of neoplasm or renal disease, 10 patients with pernicious anemia in relapse, and 10 with pernicious anemia in remission. The urine was collected for 24 hours after the test dose, and an aliquot of each specimen was assayed in duplicate with Streptococcus faecalis to estimate the folic acid content.

The patients with pernicious anemia in relapse were given test doses of folic acid, and the urinary excretion of folic acid was determined on alternate days over a period of at least 14 days. Giving the test dose on alternate days prevented significant overlap in the increased urinary excretion of folic acid. The administration of cyanocobalamin (250 or 1,000 mcg. given intramuscularly daily for 10 days) was commenced in 8 patients after the third folic acid injection and after the first injection in the other 2. The high dosage of vitamin B_{12} was given to obtain saturation as soon as possible. These experiments were controlled by performing similar folic acid excretion tests on alternate days in 3 normal subjects and in 2 patients in complete remission induced by vitamin B_{12}. Two patients with pernicious anemia were studied in the same way as the other patients with this disease, but, instead of folic acid, test doses of 3 mg. of leucovorin (folinic acid) were used. The urinary excretions of folic acid and folinic acid were assayed with Str. faecalis and Leuconostoc citrovorum together with a differential assay.

The results of the various tests are presented in tables, including the excretion of material with only folic acid-like activity (pteroylglutamic acid [P. G. A.]) and that assayable with L. citrovorum (citrovorum factor [C. F.]) in the 2 patients given leucovorin test doses. Summarizing their observations, the authors say that, with a folic acid excretion test, evidence of a deficiency of folic acid was found in 5 out of 10 patients with pernicious anemia. The degree of unsaturation appeared to be slight, and probably does not contribute to the dyshematopoiesis of pernicious anemia. In patients treated with cyanocobalamin, a reduced excretion of P. G. A. and C. F. occurred after administration of either 5 mg. of folic acid or 3 mg. of leucovorin. The changes in the nature and rate of the hematopoiesis were not solely responsible for this fall, since in all but 2 patients they occurred after the reticulocyte peak.

Failure of Ristocetin Therapy in Three Cases of Staphylococcal Sepsis with Bacteremia. L. A. Rantz and E. Jawetz. New England J. Med. **259**:963-966 (Nov. 13) 1958 [Boston].

Ristocetin is a new antimicrobial agent produced by Nocardia lurida, of large molecular size and active against gram-positive bacteria. It has been stated to be effective in the treatment of enterococcic and staphylococcic endocarditis. The manufacturer's brochures suggest that it is bactericidal for staphylococci and that patients with severe disease caused by these organisms may be expected to benefit from its administration. Studies in vitro by one of the authors, described here, and by others previously demonstrate that this is not a bactericidal drug, and very few published data are available to substantiate its clinical efficacy. The authors present the histories of 3 patients with staphyloccic sepsis with bacteremia whom they treated with

ristocetin. Bacteremia persisted in each during therapy, and clinical improvement failed to occur. The serum of 2 patients was bacteriostatic and bactericidal for the causative organism at the very time that it could still be isolated from the blood. Clinical improvement did not occur in any patient, and in one there was a substantial deterioration in the condition while 2 Gm. of ristocetin was being administered daily.

These treatment failures in patients with infections caused by staphylococci apparently as sensitive to the action of ristocetin in vitro as strains examined by other investigators, and, in fact, inhibited and killed by the serum of the patients during treatment, suggest that a serious and unknown defect in the mode of action of this drug must protect the micro-organism from its effects. It was first thought that this might be due to serum binding, but this could not be demonstrated in vitro. The complete failure of response in 3 patients with staphylococcic sepsis does not suggest that it will be of great value in the management of this disease. Better results were obtained in each case by appropriately selected combinations of other antimicrobial agents, and the infection was eradicated in 2 by this technique.

The Treatment of Constipation with the Use of Antibiotics. A. Ravina. Presse méd. **66**:1649-1650 (Oct. 25) 1958 (In French) [Paris].

The author found that several antibiotics, especially tetracycline and neomycin, had results superior to those of ordinary laxatives in the treatment of constipation and can even cure it. Posology is related to results obtained. The author suggested 1 Gm. of tetracycline daily for 5 to 7 days, 500 mg. for the same length of time, and then 250 to 500 mg. twice a week. Effects were usually seen 3 or 4 days after the beginning of treatment. It was rarely necessary to continue treatment for more than a month. Other antibiotics used were Rovamycin (in moderate initial doses), Oleandomycin, Cathomycin, Aureomycin, and Terramycin. When diarrhea occurred, 5 to 10 Gm. of bismuth subnitrate and small amounts of antispasmodic drugs were added to the treatment. Antibiotic medication for constipation was well tolerated. Long experience showed that fears of digestive disturbance due to bacteriolytic substances and of the appearance of a microbial resistance which could impair the action of antibiotics in case of serious infections were groundless. Doses were small enough so that digestive disorder rarely followed. The types of constipation that accompany acne rosacea and dolichocolon or megacolon were especially responsive to this treatment. Cures were complete and prolonged. Even after a short-term antibiotic treatment the volume of feces was considerably increased in a large number of cases.

Further research is needed to define the mode of action of this antibiotic therapy. It is suggested that the effect is due to a modification of the intestinal peristalsis in those patients who have a more serious colonic stasis than was presumed. The author believes that the explanation can more reasonably be based on profound modifications of the intestinal flora.

PATHOLOGY

Hemorrhagic States Secondary to Intravascular Clotting: An Experimental Study of Their Evolution and Prevention. G. D. Penick, H. R. Roberts, W. P. Webster and K. M. Brinkhous. A. M. A. Arch. Path. **66**:708-713 (Dec.) 1958 [Chicago].

The paradoxical sequence of clotting followed by hemorrhage develops in certain hemorrhagic complications of pregnancy, surgical trauma, burns, etc. This investigation was conducted to determine whether animals with comparably defective clotting system would be protected from the effects of intravenously administered thromboplastin. The responses of these animals to injected thromboplastin were compared with those of normal control dogs. Crude tissue extracts, which are regarded as "complete" thromboplastin, were injected into 2 normal and 2 hemophilic dogs. Shortly all the animals exhibited minor convulsive movements, hyperpnea, cyanosis, nystagmus, and excessive salivation. The reaction in the hemophilic dogs was less severe and less prolonged than that in the normal animals. All the dogs exhibited thrombocytopenia, hypofibrinogenemia, hypoprothrombinemia, and depressions in the antihemophilic activity of the plasma. These responses were diminished or were nonexistent in dogs with hypocoagulable blood. A similar reaction took place after injection of ultracentrifuged preparations of thromboplastin, which are regarded as "partial" thromboplastin, into a normal and a hemophilic dog. After injection the normal dog showed signs of respiratory difficulty, hyperkinesis, excessive salivation, and tachycardia. Prothrombin concentration was not appreciably altered in either animal. The fibrinogen level decreased in the normal dog but did not change significantly in the hemophilic dog. Depression in the antihemophilic activity of the plasma occurred in the normal dog. Thromboplastin injection prolonged the prothrombin time of the plasma in 4 other normal dogs; no changes were noted in the hemophilic dog.

Partial thromboplastin was injected into each of 4 dogs treated with bishydroxycoumarin (Dicumarol) and into 2 normal dogs. Both normal animals developed respiratory difficulty, hyperkinesis, tachycardia, and pupillary dilation. The animals treated with Dicumarol showed no overt response. In the normal dogs transient thrombocytopenia, hypopro-

thrombinemia, hypofibrinogenemia, and secondary hemophilia were manifest. These changes were less pronounced in the animals treated with Dicumarol. Partial thromboplastin was injected into 4 dogs to which chloroform had been administered by inhalation 48 hours earlier. Two normal control dogs were studied at the same time. The normal animals again showed reaction signs similar to those described previously. The chloroform-treated animals, even when given up to 6 times as much thromboplastin as the normal dogs, showed no apparent response. Chloroform administration alone had produced low levels of prothrombin and of fibrinogen and depressed the antihemophilic activity of the plasma in all 4 dogs to about 45% of the levels before chloroform treatment. These findings indicate similarity between the response to injected thromboplastin and the reactions known to occur during in vitro coagulation. They tend to support the concept that the hemorrhagic states in disorders associated with circulating thromboplastic tissue products probably result from widespread intravascular coagulation and concomitant consumption and depression of many clotting factors.

Staphylococcal Infection Resistant to Chloramphenicol, Erythromycin, and Novobiocin: Effect of Antibiotic Combinations on the Emergence of Resistant Strains. M. Barber, A. Csillag and A. J. Medway. Brit. M. J. **2:**1377-1380 (Dec. 6) 1958 [London].

In an attempt to combat the adaptability of Staphylococcus organisms to antibiotics, the authors introduced into a large general hospital in London a policy for the control of antibiotics, the essential items of which were abandonment of penicillin, except in certain wards of the hospital, and use of 2 antibiotics in combination wherever possible and always when erythromycin or novobiocin was used. The antibiotic sensitivity of all strains of Staphylococcus pyogenes var. aureus isolated from patients with infectious diseases in the hospital was studied during 6 months before the introduction of this policy in April, 1958, and for 6 months afterwards.

Analysis of erythromycin-and-chloramphenicol-resistant infections showed evidence of cross-resistance between these two antibiotics. Of 23 erythromycin-resistant strains, 11 came from patients who had been treated with chloramphenicol; 8 of the 11 patients had been given chloramphenicol in combination with erythromycin and 3 had received chloramphenicol without erythromycin. Moreover, 8 of the erythromycin-resistant strains also showed resistance to chloramphenicol, although in 2 cases the patient had been treated with erythromycin but not chloramphenicol. No such cross-resistance was noted between erythromycin and novobiocin, and of 108 patients treated with this combination, none yielded a Staphylococcus organism resistant to erythromycin, although from 2 of these patients strains resistant to novobiocin were isolated. These findings emphasize the danger of erythromycin-resistant infection becoming a hospital problem if the unrestricted use of erythromycin is permitted. Since there is evidence of cross-resistance between erythromycin and chloramphenicol, combined treatment with these 2 antibiotics offers no solution. Since novobiocin, like erythromycin, has the defect that staphylcocci readily become resistant to it, both should be used sparingly, and neither except in combination with the other or with another chemotherapeutic agent.

Two Serological Tests for Staphylococcal Infection. A. G. Towers and G. P. Gladstone. Lancet **2:**1192-1195 (Dec. 6) 1958 [London].

Serums obtained from 156 patients, 83 of whom had staphylococcic infections and 73 had other infections, were examined for their content of anti-Panton-Valentine (P.V.) leukocidin during the course of infection, and the results were compared with those of anti-alpha-hemolysin tests. Of the 83 patients, 69 had osteomyelitis, 6 had tuberculous sinuses secondarily infected by staphylococci, and 8 had other stapyhlococcic infections. Of the 73 patients, 22 had bone and joint tuberculosis, and 51 had miscellaneous nonstaphylococcic infections. A rise of titer of anti-alpha-hemolysin was found in only 27 (33%) of the 83 patients with staphylococcic infections, whereas the titer of anti-P.V.-leukocidin was raised in 68 (82%) of the 83 patients. On the other hand, 12 (17%) of the 73 patients with other infections had an increased anti-P.V.-leukocidin serum level, whereas none of them had an increased anti-alpha-hemolysin serum level. A combination of these 2 serologic tests is of diagnostic value, particularly in patients with deep-seated infection from whom no organisms have been isolated, because the organisms often multiply in sites from which recovery is difficult, such as spinal lesions.

Seminiferous Tubule Dysgenesis (Klinefelter's Syndrome) in Identical Twins. D. A. Holub, M. M. Grumbach and J. W. Jailer. J. Clin. Endocrinol. **18:**1359-1368 (Dec.) 1958 [Springfield, Ill.].

Seminiferous tubule dysgenesis (Klinefelter's syndrome) was proved by testicular biopsy in 17-year-old identical twins who presented with the

typical clinical features of the syndrome. Female nuclear chromatin patterns were present in the Leydig cells and in buccal mucosal smears of both patients. The identity of the twins was established by means of reciprocal homografts, blood antigen studies, dermatoglyphics, and the history of a single placenta. The principal theories concerning the etiology of this syndrome are briefly reviewed. It is concluded that concordance for seminiferous tubule dysgenesis in identical twins in the light of previous evidence supports the concept that a genetic predisposition exists in this disorder.

ANESTHESIA

Procaine Sensitivity: The Relationship of the Allergic Eczematous Contact-Type to the Urticarial, Anaphylactoid Variety: The Use of Xylocaine in Procaine-Sensitive Individuals. A. A. Fisher and H. M. Strum. Ann. Allergy **16**:593-598 (Nov.-Dec.) 1958 [St. Paul].

The authors found that allergic eczematous sensitivity to procaine, besides being an occupational hazard of the dental profession, is fairly common in the general population. They found 36 patients who showed strongly positive reactions to patch tests with 2% aqueous solution of procaine hydrochloride. Recently they were able to confirm the observations of others that many individuals who have allergic eczematous sensitivity to products of the group embracing paraphenylenediamine, benzocaine, and para-aminobenzoic acid frequently show cross-reactions to procaine. Since paraphenylenediamine and benzocaine are among the more common and most potent sensitizers, it becomes apparent that procaine sensitivity may become established in many patients who have never had actual topical contact with procaine. In addition, it must be remembered that procaine is the most widely used local anesthetic. While it is generally admitted that procaine frequently causes eczematous contact allergy, there seems to be no agreement as to the frequency with which it causes urticarial anaphylactoid allergy. In this paper the authors describe experiments carried out to obtain more accurate information concerning the hazards of the injection or ingestion of procaine in patients with allergic eczematous contact-type sensitivity to procaine.

Twenty patients with allergic eczematous sensitivity to procaine were subjected to scratch and intradermal tests, subcutaneous injections, and ingestion of procaine. None of these patients showed immediate local wheal reactions to these tests, and none had general urticarial or anaphylactoid reactions. As a rule, it would seem that allergic eczematous sensitivity to procaine is not accompanied by the vascular, anaphylactoid allergy, certainly not to any notably high degree. Xylocaine has proved an excellent substitute for, and does not cross-react with procaine. Dentists with eczematous sensitivity to procaine can use Xylocaine without skin reaction. Although urticarial anaphylactoid sensitivity rarely accompanies eczematous sensitivity to procaine, it would nevertheless seem wise to use Xylocaine for local anesthesia in all persons sensitive to procaine.

Clinical Evaluation of a New Ultrashort-Action Oxygen Barbiturate for Intravenous Anesthesia. R. Weyl, B. Unal and Y. Alper. Surg. Gynec. & Obst. **107**:588-592 (Nov.) 1958 [Chicago].

The authors report clinical observations on 200 unselected patients in whom anesthesia was induced with the new ultrashort-acting oxybarbiturate, methohexital sodium, also known as compound 25398. Chemically it is 1-methyl-5-allyl-5 (1 methyl-2-pentynyl) sodium barbiturate. It is a white crystalline solid which is easily soluble in water. It is stable in aqueous solution at 5 C for 1 year and at 25 C for 6 months. The pH ranges between 10 and 11. Preliminary studies carried out by others on cats, mice, rabbits, monkeys, and dogs showed the compound to be 3 times as potent and one-half as long in action as thiopentobarbital (thiopental sodium) and much less likely to show accumulation. The compound did not produce venous irritation or hemolysis during these animal experiments.

The authors found that in the 200 patients the new ultrashort-acting methohexital sodium provided smooth rapid induction, adequate maintenance, and prompt awakening with the use of either a 1% solution for intermittent intravenous injection or a 0.2% solution for intravenous drip. The required doses of this drug are small as compared with those of the thiobarbiturates. The drug seems to be metabolized quickly. It supplies good jaw relaxation, so that a pharyngeal airway can be introduced early. Laryngospasm did not occur in this series. The compound provided an adequate state of analgesia; this was best achieved by the slow-drip method. The compound could be used in connection with the usual inhalants and relaxants. No convulsions occurred in this series, and no venous irritation was noted at the site of injection. Compound 25398 seems to be a safe agent in the hands of the experienced anesthetist. It deserves further evaluation.

BOOK REVIEWS

Penicillin. By Harold L. Hirsh, M.D., and Lawrence E. Putnam, M.D. Foreword by Harry F. Dowling, M.D. Antibiotics monographs no. 9. Under editorial direction of Henry Welch, Ph.D., and Féliz Marti-Ibáñez, M.D. Cloth. $4. Pp. 148, with 9 illustrations. Medical Encyclopedia, Inc., 30 E. 60th St., New York 22; Distributors outside U. S. A.: Interscience Publishers, Inc., 250 Fifth Ave., New York 1; Interscience Publishers, Ltd., 88-90 Chancery Lane, London, W. C. 2, England, 1958.

The authors of this monograph have imparted a wealth of highly practical information obtained over a 15-year period of firsthand experience with penicillin. The slant of the book is clinical rather than pharmacological. After a brief historical introduction the antimicrobial spectrum of penicillin is discussed. This chapter identifies those areas in which penicillin is of proved value and points out those infections against which it is clearly ineffective and hence not indicated. Practical suggestions are also given for reducing the incidence of hospital-acquired infections due to penicillin-resistant strains of staphylococci. The clinical aspects of the pharmacology and toxicity of penicillin are briefly but competently presented. The chapter on dosage forms contains useful information on the characteristics of the diverse commercial preparations. The remainder of the book is devoted to a discussion of the use of penicillin in specific infections known to respond to its antimicrobial action. Each section is prefaced by a brief characterization of the particular disease and is followed by recommendations as to the preparation of choice, preferred route of administration, and proper dosage. There is a subject index and a bibliography. Since penicillin is used in practically all branches of clinical medicine, this monograph should be a valuable reference source as well as a manual of therapy for all physicians.

Urology in General Practice. By Frank Coleman Hamm, M.D., M.S., F.A.C.S., Professor of Urology, Department of Surgery, State University of New York Downstate Medical Center, Brooklyn, and Sidney R. Weinberg, M.D., F.A.C.S., Assistant Professor of Urology, Department of Surgery, State University of New York Downstate Medical Center. Paper. $6. Pp. 293, with 259 illustrations [drawings] by Elizabeth Cuzzort. J. B. Lippincott Company, E. Washington Sq., Philadelphia 5; 4865 Western Ave., Montreal 6, Canada, 1958.

The authors state that, after using this book for a year in their classes at the State University of New York, they have been encouraged by the response of students and other teachers to make it available for wider distribution. Although the book is paper-backed the print and paper are excellent and the illustrations are clear and instructive. The aim of this book is to introduce the medical student and the resident to the field of urology, and to provide a ready reference in the subject for those in other branches of medicine and surgery. The principles of management presented are generally accepted. The material is well arranged and adequately illustrated. This is one of the best of many similar texts on urology which have been published in the United States in the past three years.

The Ecology of the Medical Student: Report of the Fifth Teaching Institute, Association of American Medical Colleges, Atlantic City, New Jersey, October 15-19, 1957. Edited by Helen Hofer Gee and Robert J. Glaser, with assistance of Planning Committee. Editorial coordination by E. Shepley Nourse. Published as part 2 of Journal of Medical Education, October, 1958. Cloth. $3. Paper. $2. Pp. 262, with illustrations. Office of Director of Research, Association of American Medical Colleges, 2530 Ridge Ave., Evanston, Ill., 1958.

In the introduction to this comprehensive report Dr. G. P. Berry points out that "becoming a good doctor is one of the most difficult things in the world." The Institute on the Ecology of the Medical Student focused attention on the various stresses that influence the growth and development of the modern physician. The first part of the report treats the characteristics of medical schools and medical students, dealing with the diversity of values and objectives in medical education and the implications of this diversity. The need for intelligent planning in medical education is stressed as well as the need for research into personality development in interactions with the medical school environment. The second section points up certain factors affecting medical students such as the educational environment, noncurricular factors, and student counseling.

The third section presents interesting data on sociological contributions to the study of the medical student, presenting the procedures for the sociological study of the value climate of medical schools, a commentary on medical education in the social sciences, and an analysis of the development of professional attitudes and capacities. The final section deals with educational patterns in medicine today. It presents new directions in programs of medical education, traditional as opposed to novel approaches to medical education, and the place of the student in the British pattern of medical education. This report is a storehouse of valuable material of vital interest and concern to educators in general, as well as to those specifically concerned

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

with medical education. At this transitional stage of medical education the sociological contributions to the problem as reported in this volume are of particular importance.

Practical Leads to Puzzling Diagnoses: Neuroses That Run Through Families. By Walter C. Alvarez, M.D., D.Sc. Cloth. $9. Pp. 490. J. B. Lippincott Company, E. Washington Sq., Philadelphia 5; 4865 Western Ave., Montreal 6, Canada; Pitman Medical Publishing Company, Ltd., 39 Parker St., London, W. C. 2, England, 1958.

The author briefly summarizes his purposes and objectives as follows: "In this book I describe the symptoms and the syndromes which I found bothering 574 relatives of the psychotic and the alcoholic and 99 relatives of the epileptic. A number of these troubles appeared in such high percentages of the cases that they represent minor equivalents of psychosis and epilepsy. Certain it is that in the families with a poor nervous inheritance I have kept finding a remarkable amount of chronic and often life-long nervous illness, with constitutional inadequacy, neurocirculatory asthenia, hypochondriasis, unemployability, alcoholism and the habit of illness. I am left with the strong impression that these tendencies to illness are inherited." Even though the author professes his conclusions to be only impressions, his fervor makes him write as though it is an established fact that descendants of families with mental illness and alcoholism pass defective genes for the nervous system to their offspring. Environment is so casually mentioned that one has to retain many reservations regarding the authoritativeness of the context of the book. The author's list of symptoms of the relatives of the mentally ill includes practically every symptom of which patients can complain. He does not compare these with the percentages of these symptoms of which relatives of patients with carcinoma, heart disease, diabetes, or multiple sclerosis might complain. Over half of the symptoms which he lists occurred in 5% or less of the relatives, which hardly seems to be statistically significant. One's primary impression is that the book is medical fiction and has to be read with many questions in mind. It is doubtful that there is enough established fact in the text to be of much aid in resolving the puzzling problems of clinical practice.

Poliomyelitis: Papers and Discussions Presented at the Fourth International Poliomyelitis Conference. Compiled and edited for International Poliomyelitis Congress. Cloth. $7.50. Pp. 684, with 422 illustrations. J. B. Lippincott Company, E. Washington Sq., Philadelphia 5; 4865 Western Ave., Montreal 6, Canada, 1958.

The Fourth International Poliomyelitis Conference was held in Geneva, Switzerland, in 1957. As was the case after the preceding conferences the demand for a permanent record of the papers and discussions necessitated the publication of this book. It is dedicated to Franklin D. Roosevelt and Prof. Edmond Grasset, both dead. It is to be hoped that the subject itself will enter the realm of past history soon. At this conference interest was centered on vaccination against poliomyelitis, enteric viruses that cause poliomyelitis-like diseases, cultures of mammalian cells, new diagnostic techniques, group and home care of patients with poliomyelitis, and the treatment of the severely stricken. The book is well illustrated with photographs and diagrams. Many of the papers have summaries and lists of pertinent references, and a general summation is presented at the end. The book is well printed and contains an index.

General Ophthalmology. By Daniel Vaughan, M.D., Assistant Clinical Professor of Ophthalmology, University of California School of Medicine, San Francisco, Robert Cook, M.D., Clinical Instructor, Department of Ophthalmology, University of California School of Medicine, and Taylor Asbury, M.D., Assistant Professor of Ophthalmology, College of Medicine, University of Cincinnati, Cincinnati, Ohio. Paper. $4.50. Pp. 328, with illustrations by Ralph Sweet. Lange Medical Publications, Los Altos, Calif., 1958.

From the first pages, where the differential diagnosis of common causes of the inflamed eye is clearly outlined, through the excellent index and selected bibliography the authors present a concise, up-to-date outline of ophthalmology. This work should be of great value in the diagnosis and treatment of eye diseases, not only to the medical student, general practitioner, pediatrician, internist, and resident in ophthalmology but also to the practicing ophthalmologist. The work is authoritative and reveals the skilled hands of Dr. Phillips Thygeson and Dr. Frederick Cordes, to whom the authors give much credit. The chapter on examination is well done and describes some of the more recent methods of diagnostic examination of the eye. Of particular value to the practicing physician is the chapter on the management of common ocular disorders. The sections on ocular emergencies in glaucoma are exceedingly important for the general practitioner. The authors stress the need for the cooperation of physicians in measuring intraocular tension during routine physical examinations in order that much of the unrecognized glaucoma may be diagnosed early and treatment instituted before irreversible ocular damage occurs.

Although there are no colored illustrations in the book, the black and white drawings and photographs are so excellent that except in the chapter on ocular disorder associated with systemic diseases the absence of color is unimportant. The chapter on trauma is brief but excellent and should be read by all who have to deal with ocular emergencies. It is especially recommended to the industrial surgeon. Chapter 13 (on neuro-ophthalmology) gives a brief but valuable outline of the subject which should be helpful to neurologists and neurosurgeons. The publishers have done a fine piece of work but ease and speed of reading might

be facilitated if there were two columns to a page. This book is enthusiastically recommended to all who wish a clear, concise review of the essentials of ophthalmology.

Medical Department, United States Army: Preventive Medicine in World War II. Volume IV: Communicable Diseases Transmitted Chiefly Through Respiratory and Alimentary Tracts. Prepared and published under direction of Major General S. B. Hays, Surgeon General, United States Army. Editor in chief: Colonel John Boyd Coates Jr., MC. Editor for preventive medicine: Ebbe Curtis Hoff, Ph.D., M.D. Assistant editor: Phebe M. Hoff, M.A. Office of the Surgeon General, Department of the Army, Washington, D. C. Cloth. $5.50. Pp. 544, with illustrations. Superintendent of Documents, Govern. Print. Off., Washington 25, D. C., 1958.

This volume is a part of the clinical as distinguished from the administrative series on the history of the Medical Department of the Army in World War II. Two previous volumes on preventive medicine have been published. After an introductory chapter by Dr. John E. Gordon there are sections on diseases transmitted through the respiratory and alimentary tracts. Among others Dr. Joseph Stokes contributed chapters on chicken pox, mumps, measles, rubella, and pertussis; Dr. Philip Sartwell one on common respiratory diseases; Dr. Thomas Francis Jr. one on influenza; Dr. Joseph Smadel one on psittacosis; Col. L. A. Potter one on smallpox; Dr. A. C. McGuiness one on diphtheria; Dr. Esmond Long one on tuberculosis; Dr. Dwight Kuhns one on salmonelloses; Dr. Gail Dack one on food poisoning; and the late Gen. R. A. Kelser one on brucellosis. This partial list of contributors gives some idea of the high quality of the work. It is a great pity that we have had to wait so long for this volume and it hoped that the other volumes in this series will appear soon. The book has an index.

Rehabilitation Medicine: A Textbook on Physical Medicine and Rehabilitation. By Howard A. Rusk, M.D., Professor and Chairman of Department of Physical Medicine and Rehabilitation, New York University–Bellevue Medical Center, New York, and 36 collaborators. With editorial assistance of Eugene J. Taylor, A.M. Cloth. $12. Pp. 572, with 172 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1958.

Dr. Rusk and co-workers have attempted to cover a broad field within the confines of a relatively small book. They believe that the treatment of almost every type of illness, with the exception of minor injuries and simple acute infections, involves the process of rehabilitation. Part 1 deals with the principles of rehabilitation and part 2 with the application of these principles to specific disease problems. This book can be read with profit by the general practitioner or the specialist. Great emphasis has been placed on readability, and for this thanks is probably due Eugene J. Taylor, who is listed as an editorial assistant. The discussion of the principles of rehabilitation sums up everything the authors have talked and written about since the establishment of their service. It should provide an invaluable point of reference for these ideas, which are now collected for the first time under one cover. The fact that the emphasis on the activities of daily living as the focal point for rehabilitative therapy now seems so simple and familiar is almost entirely due to Dr. Rusk's persistence in forcefully supporting this concept.

The sections on electrodiagnosis and electrotherapy bring together many items formerly widely scattered. The chapter on writing prescriptions for rehabilitative treatment should be required reading for all physicians. The chapter on management of psychiatric problems is also excellent. It is hoped that in future editions the authors will eliminate the extended discussion of such an outmoded modality as ultraviolet ray therapy for the many conditions for which it is now recommended. In the discussion of the goniometer there is an apparently inadvertent omission of the method for determining the center of motion of a joint before attempting to measure the range of motion. The possible error is great when this point is neglected. The format of the book is conventional and attractive. There are many excellent photographs and useful charts.

Cyclopropane Anesthesia. By Benjamin Howard Robbins, B.A., M.S., M.D., Professor of Anesthesiology and Associate Professor of Pharmacology, Vanderbilt University School of Medicine, Nashville. Second edition. Cloth. $9. Pp. 293, with 74 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2, 1958.

This edition comes 18 years after the first. The author believes that this is the time for another unified discussion of the subject since there is an apparent increase in the use of cyclopropane in clinical anesthesiology in the United States. This monograph is a reference work and should not be considered a clinical textbook. Its bibliography is extensive, containing 353 references. After a description of the physical and chemical properties and listing the concentrations of cyclopropane needed for anesthesia and respiratory arrest, 110 pages are devoted to its effect on the circulatory system. This is the most extensive discussion in the book and reviews the literature at length. Other chapters discuss the effects of cyclopropane on the respiratory and gastrointestinal systems, the blood, and other tissues. The chapter on clinical administration includes descriptions of techniques that have been reported in the literature.

The author chose to include a short chapter on the relaxing agents because "the introduction of the relaxing agents in 1942 and the widespread use of one of them at the present time makes the use of cyclopropane even more satisfactory." He found no contraindications to the use of cyclopropane

except where the explosion hazard (x-ray or cautery) is encountered and in circumstances where epinephrine will be used. The final chapter discusses the explosion hazard with cyclopropane. This monograph will be used by teachers and advanced students. It will not be of value to medical students or others with little clinical experience with cyclopropane. It is attractively composed and printed.

Chloromycetin (Chloramphenicol). By Theodore E. Woodward, M.D., and Charles L. Wisseman Jr., M.D. With collaboration of Harry M. Robinson Jr., M.D., and others. Foreword by Joseph E. Smadel, M.D. Antibiotics monographs no. 8. Under editorial direction of Henry Welch, Ph.D., and Félix Martí-Ibáñez, M.D. Cloth. $4. Pp. 159, with 19 illustrations. Medical Encyclopedia, Inc., 30 E. 60th St., New York 22. Distributors outside U. S. A.: Interscience Publishers, Inc., 250 Fifth Ave., New York 1; Interscience Publishers, Ltd., 88-90 Chancery Lane, London, W. C. 2, England, 1958.

This book is the eighth in a series of monographs published under the direction of the editors of Antibiotics Annual. The authors have produced a highly readable and selective review of the important studies that have been made concerning chloramphenicol, the first of the broad-spectrum antibiotics. There are chapters on the history, activity, properties, dosage forms and route of administration, side-effects, and the clinical results obtained in various infections. Pertinent information is included on the use of other antibiotics and drugs in chloramphenicol-susceptible infections. There is an extensive bibliography and a subject index. As a whole, this monograph should give most readers a balanced picture of the place which chloramphenicol has come to occupy in the treatment of microbial diseases. It should also be of particular value as a reference to and source of information about the drug.

Myasthenia Gravis. By Kermit E. Osserman, M.D., F.A.C.P., Physician-in-Charge, Myasthenia Gravis Clinic, Mount Sinai Hospital, New York. Cloth. $10. Pp. 286, with 58 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 15/16 Queen St., Mayfair, London, W. 1, England, 1958.

A modern monograph on myasthenia gravis has been needed and is now provided by a physician who has had personal experience with more than 350 cases. Although not a common disease, it is being recognized with increasing frequency and, by its nature, it occupies a central position in the differential diagnosis of neurological disorders. With the decline of poliomyelitis it has become one of the most common causes of respiratory paralysis. The illustrations are clear and pertinent. A large number of references are given at the close of each chapter, and there is an adequate index. In this volume the author provides a comprehensive view of this disorder. Normal and abnormal functions of the neuromuscular junction, clinical features, diagnosis, and therapy by means of drugs and thymectomy all receive detailed attention. Much of the material has been published previously by the author but it is useful to have it collected in one volume. An excellent chapter on pathology is provided by Dr. Harvey Mendelow.

The author has performed a great service, but his conclusion must be accepted with some reservations because he is a therapeutic enthusiast. At the outset he states: "particularly in the last five years, new drugs and techniques of management have given the physician tools with which to make the myasthenic patient lead a more normal life." In discussing one of these new drugs, Mestinon, the author reports changes in the economic usefulness of his own patients and claims that "various clinics report up to 70 to 75 per cent increased clinical improvement (on Mestinon) as compared to Prostigmin," but examination of the reports cited does not bear out this contention. Many workers believe that the administration of the new drugs (Mestinon, Mytelase, or any of various experimental preparations) rarely makes a myasthenic patient significantly better than he was under therapy with neostigmine, which has been available since 1935. The value of the new drugs lies chiefly in the facts that their effects are more prolonged or the side-effects are less pronounced. The latter are usually evaluated according to the patient's statement rather than any objective criteria. The use of these drugs has not appreciably affected the mortality of the disease (15 to 30%), nor have they helped in establishing the indications for thymectomy. The author recommends the use of his edrophonium test to determine whether the patient is receiving adequate medication. This test has been widely accepted as a means of differentiating cholinergic from myasthenic crisis, although it has not yet been subjected to critical analysis or controlled study. Its value is not proved in the present monograph beyond the statement that "it is invaluable." Despite minor reservations of this nature, the monograph should be useful to the internists and neurologists who are responsible for the care of patients with myasthenia gravis.

Acetophenetidin: A Critical Bibliographic Review. By Paul K. Smith, Ph.D., Professor of Pharmacology, George Washington University School of Medicine, Washington, D. C. Monographs of Institute for Study of Analgesic and Sedative Drugs IV. Cloth. $5.75. Pp. 180, with 11 illustrations. Interscience Publishers, Inc., 250 Fifth Ave., New York 1; Interscience Publishers, Ltd., 88-90 Chancery Lane, London, W. C. 2, England, 1958.

This book presents a critical review of the literature on the well-known analgesic-antipyretic agent acetophenetidin and its major metabolite N-acetyl-*p*-aminophenol (*p*-hydroxyacetanilid), to which the nonproprietary names acetaminophen and paracetamol have been applied. The book includes comments by the author as well as abstracts

from the literature and from unpublished data. The main text covers the drug's history, chemistry, fate and metabolism in the body, antipyretic and analgesic actions, other therapeutic uses, effects on blood and other tissues, toxicology, tolerance, and habituation, and a summary. The bibliography and a general index appear at the end of the book. In addition to reviewing data pertaining only to acetophenetidin, the literature abstracted also includes studies of its comparative and/or combined action with such other drugs as aminopyrine, antipyrine, allylbarbituric acid, amobarbital, aspirin, salicylamide, and neocinchophen. This monograph should be of special interest and use to pharmacologists and clinical investigators as a critical guide to previously reported studies of the subject drug.

The Health of a Nation: Harvey W. Wiley and the Fight for Pure Food. By Oscar A. Anderson Jr. Published with aid from Charles Phelps Taft Memorial Fund, University of Cincinnati. Cloth. $6. Pp. 333, with illustrations. Published for University of Cincinnati by University of Chicago Press, 5750 Ellis Ave., Chicago 37; Cambridge University Press, Bentley House, 200 Euston Rd., London, N. W. 1, England; University of Toronto Press, Toronto 5, Canada, 1958.

This book deals with Harvey W. Wiley, M.D., who made a major contribution to the health of the United States. It should be of particular interest to students of the developments which led to the enactment of the laws which now serve to safeguard our food and drug supplies. The problems and controversies which confronted Dr. Wiley are ably presented. The author acknowledges the constructive part played by the American Medical Association and by individual physicians in the struggle to advance the public interest. Dr. Wiley, food adulteration, and claims for the alleged values of some medicines were and still are highly controversial topics. The book is a valuable contribution to an important field of public health history, even though some students may hold that the author's portrayal of Dr. Wiley's dynamic individualism is not all that he deserves.

The Recovery Room: A Symposium. By John Adriani, M.D., Professor of Surgery, School of Medicine, Tulane University, New Orleans, and John B. Parmley, M.D., Instructor in Surgery, School of Medicine, Tulane University. Publication number 340, American Lecture Series, monograph in American Lectures in Anesthesiology. Edited by John Adriani, M.D., Director, Department of Anesthesia, Charity Hospital, New Orleans. Cloth. $4.25. Pp. 123, with 17 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

In this symposium on nursing and administration in anesthesiology the authors discuss, by means of questions and answers, the definitions, purpose, location, physical setup, administration, personnel, equipment, economics, policies and procedures, general patient management, and special problems of the subject. The illustrations are neat and easily read. This book should be available to nurses, interns, and residents in anesthesiology and surgery. It is neatly and simply organized and approaches the problem directly. Probably the greatest value of this book would be to those organizing a recovery room for the first time. Here they would quickly find the answer to most of their questions.

The Care of the Geriatric Patient. Edited by E. V. Cowdry, Ph.D., Sc.D., Director of Wernse Cancer Research Laboratory, Washington University School of Medicine, St. Louis. Cloth. $8. Pp. 438. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1958.

Care of the geriatric patient has become a prominent subject in the medical literature. This monograph begins with five lectures given to the Los Angeles County Medical Association in 1955, with the addition of discussions of various aspects of management of geriatric patients. Generally, it should serve as a reference book for anyone who treats elderly patients. This phase of patient care should be the function of all doctors and should not be classed as a specialty. This book is comprehensive and goes into various subjects thoroughly; indeed, it may embrace too much with regard to the various specialties. It is heartening to see included a discussion of care of the patient in his home because this aspect has heretofore been neglected. There is an excellent chapter on rehabilitation. Although the philosophy of the book is good, it is hoped that it will not make the reader think he has to be a specialist to care for elderly patients. This monograph should be added to the many books on this subject as a reference for the interested physician. One might wish that it were shorter, because it is doubtful that the busy physician will read it as thoroughly as he should.

Temporal Lobe Epilepsy: A Colloquium Sponsored by the National Institute of Neurological Diseases and Blindness, National Institutes of Health, Bethesda, Maryland, in Cooperation with the International League Against Epilepsy. Edited by Maitland Baldwin and Pearce Bailey. Co-editors: Cosimo Ajmone-Marsan, Igor Klatzo, and Donald Tower. Cloth. $15.50. Pp. 581, with illustrations and 1 chart in back pocket. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

It is not long since the temporal lobes, especially the right one, were counted among the more "silent" areas of the brain. Now they constitute one of the more fruitful fields for neurological investigation. Because they excite the interest of specialists in neurology, psychiatry, neurosurgery, anatomy, chemistry, endocrinology, pathology, electroencephalography, psychology, and other fields, there has sprung up in recent years a vast literature dealing with this portion of the brain. It is most valuable to have available authoritative summaries to

which one not familiar with the field or without the time for fuller research may turn for information. This book is such a summary. It is a collection of the papers and the discussion presented at Bethesda, Md., in March, 1957. Those taking part in this symposium constituted most of the outstanding investigators in the world who have interested themselves in these problems. Their papers vary from extensive analyses of the material available to them to brief summaries of two or three pages. They represent many different viewpoints and opinions. The papers have been well prepared and are clear and concise. The discussion has been well edited without losing the spontaneity and often the sparkle which must have characterized this meeting. This is not an encyclopedia, but it is an excellent source of information for those who would bring themselves up to date on this subject and also a starting point for further, more detailed reading. The typography and format are good.

Radiology for Medical Students. By Fred Jenner Hodges, M.D., Professor and Chairman, Department of Radiology, University of Michigan, Ann Arbor, Isadore Lampe, M.D., Professor, Department of Radiology, University of Michigan, and John Floyd Holt, M.D., Professor, Department of Radiology, University of Michigan. Third edition. Cloth. $8.50. Pp. 450, with 109 illustrations. Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1958.

In this edition the authors have revised and reappraised certain portions and deleted others to make room for the inclusion of materials on new developments in diagnostic and therapeutic radiology. The book is intended for the undergraduate student of medicine. It presents basic principles and a fundamental understanding of radiology. The authors, using their book at Michigan to teach juniors, have dispensed with formal lectures, thus increasing the opportunity for informal teaching by means of the case method. The acceptance of this book is attested by the demand for this new edition. The first half is devoted to diagnostic radiology and includes well-chosen illustrations. A chapter dealing with the rapidly expanding field of cardiovascular radiology has been added; the section on pediatric radiology has been accorded proper attention; and material concerned with the biological hazards of radiation has been expanded. The remainder of the book dealing with therapeutic radiology has been revised, with the addition of new material concerning the use of radioactive cobalt (Co^{60}) and reflecting the declining use of radiation in the treatment of nonmalignant disease. In the final paragraph of the preface the authors express a hope that this new edition will serve as well as, if not better than, its predecessors. This book is recommended without reservation to medical students and their teachers. The postgraduate student in radiology should also find it useful, particularly if he is training in a teaching hospital.

Polarography in Medicine, Biochemistry, and Pharmacy. By M. Brezina and P. Zuman. With foreword by J. Heyrovsky. Translated from Czech by S. Wawzonek. [English edition revised from second Czech edition.] Cloth. $19.50. Pp. 862, with 319 illustrations. Interscience Publishers, Inc., 250 Fifth Ave., New York 1; Interscience Publishers, Ltd., 88/90 Chancery Lane, London, W. C. 2, England, 1958.

In this thoroughly annotated bibliography of the literature of polarographic analysis in the fields of medicine, biochemistry, and pharmacy through 1954, theoretical considerations are touched on only briefly as are descriptions and discussions of general instrumentation. The book is intended mainly to serve the practicing analyst as a survey of the published methods and as a laboratory reference text. Most of the methods are given in sufficient detail for the experienced analyst to use without referring to the original work. About half of the references are to non-English language publications. The text is divided into sections covering the analysis of inorganic compounds, including elements and anionic groups, as determined in air, water, soil, drugs, and in plant and animal tissue. Organic compounds are classified by chemical functional group and also as biochemical classes in which are included vitamins, hormones, alkaloids, and miscellaneous steroids. Proteins and enzymes are treated separately. Tables of important buffers and of half-wave potentials are included. The book should be of great value to those engaged in the analysis of materials of biochemical interest who use the polarographic technique.

Muir's Text-Book of Pathology. Revised by D. F. Cappell, C.B.E., M.D., F.R.F.P.S., Professor of Pathology, University of Glasgow, Glasgow, Scotland. Seventh edition. Cloth. $14.50. Pp. 1201, with 733 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; Edward Arnold (Publishers) Ltd., 41-43 Maddox St., London, W. 1, England, 1958.

This new edition of a well-known text is intended primarily to meet the requirements of undergraduate medical students. Accordingly, it follows the established pattern of such textbooks. Disturbances of the circulation; inflammation; nonspecific and specific granulomas; repair and hypertrophy; disturbances of nutrition; retrogressive changes; infection, fever, and immunity; tumors; and etiological factors in tumor growth are discussed in that order. The latter chapters are devoted to special pathology of the body systems. The text is written in a lucid style. In the course of revision the author has rearranged it to incorporate new material. He emphasizes the importance of the autopsy in the teaching of pathology and the absolute necessity for experience gained through this discipline. There is a list of references. This textbook on general and special pathology meets fully the needs of the undergraduate medical student and also serves as an excellent reference source for pathologists in practice.

QUESTIONS AND ANSWERS

REHABILITATION AFTER A HEART ATTACK

To the Editor:—*A 46-year-old patient sustained a mild myocardial infarct. He had pain in the posterior chest wall but did not seek medical aid until a month later, when angina on effort became more pronounced and he complained of "skipped beats" (pulsus bigeminus and pulsus trigeminus). He was hospitalized, maintained on bed rest and quinidine therapy, and discharged after six weeks. He convalesced at home for six more weeks and now has a vocational problem. He has been offered a position 400 miles from his home. This would involve moving his family and reestablishing his home elsewhere early in 1959. He would be required to be available for night work once every two weeks. Would such a change for this patient be considered hazardous?*

M.D., Ohio.

Answer.—This patient presents a problem in rehabilitation. Initially, a month passed before he saw his physician; then he had six weeks of rest at the hospital and six additional weeks at home. He therefore has had about four months of convalescence since his original myocardial infarct. This is a sufficient period for maximum healing. Factors that would limit his activity would be increased heart size, high blood pressure, and exertional dyspnea and angina. Assuming that he has none of these, there should be no reason why he is not physically capable of taking on a new position. The required moving of his family, reestablishment of his home, and occasional night work would have no particular harmful effects. The decision must be based, in large part, on socioeconomic factors, and these are not stated. If a man has experienced a myocardial infarction and has made a fairly satisfactory recovery, there is no reason to treat him as if he were fragile. In terms of his survival, proper diet, proper weight, and adequate activity are far more valuable than oversolicitous medical conservatism.

INHALATION OF PURE OXYGEN

To the Editor:—*How long may man breathe 100% oxygen without injurious effect?*

M.D., California.

Answer.—There now exists a sizable body of information about oxygen intoxication, some of it relating to retrolental fibroplasia and other effects on infants and some relating to the effects of oxygen inhaled under pressures higher than one atmosphere by divers. A normal man can breathe pure oxygen at atmospheric pressure continuously for 14 to 24 hours before developing a mild pulmonary irritation, according to Lambertsen (Respiratory and Circulatory Actions of High Oxygen Pressure, in Proceedings of the Underwater Physiology Symposium, Publication 377, Washington, D. C., National Academy of Sciences–National Research Council, 1955, page 25). Infants are more susceptible to oxygen intoxication, and, according to Everett (*A. M. A. Arch. Ophth.* **56**:481, 1956), for all practical purposes there is no concentration of oxygen in excess of that in air that is not associated with risk of developing retrolental fibroplasia. Prolonged action of oxygen in sufficient concentration causes vasoconstriction within the brain and inhibits certain enzyme systems, in addition to the local effects on pulmonary epithelium. In mice, a striking effect on length of life is seen at a critical concentration of oxygen near 70%. Living continually in atmospheres of 20 to 70% of oxygen has little effect on the length of life of the laboratory mouse, but Gerschman and co-workers (*Am. J. Physiol.* **192**:563, 1958) found that at concentrations between 70 and 100% there is a critical point that cannot be exceeded without markedly shortening the life of the mouse.

SENSITIVITY TO LIGHT

To the Editor:—*Several years ago when sun lamps were popular, a man now in his 60's used his sun lamp quite often with the result that he not only has what resembles an x-ray burn but also has become sensitive to sunlight and even fluorescent light and television light under certain conditions. Even his office is free from sunshine. All medical evaluation otherwise gives negative results. His main complaint after exposure is that he "feels awful" and "all in." Can any preparation be used to protect him?*

M.D., New York.

Answer.—Interpretation of this problem necessitates a complex answer. If sunshine causes the patient to "feel awful," he may be suffering from porphyria of the intermittent-acute or chronic-mixed form. His urine should be examined during an acute attack for the presence of a port-wine color, coproporphyrin, uroporphyrin, porphobilin, and porphobilinogen. If porphyria is present, the ingestion of alcohol should be avoided. Also, under these circumstances the functions of the liver should

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

be investigated by appropriate tests. If the skin shows changes which are equivalent to a chronic radiodermatitis (atrophy, telangiectasia, hyperpigmentation, hypopigmentation, ulceration, keratoses, and epitheliomas), the therapeutic and prophylactic problem is different. In the latter case, the keratoses and epitheliomas should be removed, preferably by surgical excision, as dictated by clinical necessity. Surgical planing would improve the texture and appearance of the skin and would decrease the future formation of malignant and premalignant cutaneous neoplasms. Sun screens may assist in preventing further degeneration of the skin, especially after dermabrasion. An antimalarial preparation (250 to 500 mg. of chloroquine one to four times a day by mouth) may decrease photosensitization. Avoidance of sunshine, as far as is practical, should be practiced. Mechanical protection, such as the wearing of a hat and long sleeves, is to be recommended even during overcast weather. Sunbathing and exposure to reinforced solar radiation near bodies of water is contraindicated.

TRANSFUSIONS FOR PATIENTS WITH CANCER

To the Editor:—*This question relates to giving blood to patients entering the hospital in terminal or near terminal stages of carcinomatosis. These patients are not suffering any blood loss from acute gastrointestinal, pulmonary, or uterine hemorrhage. For example, a 52-year-old woman was admitted to the hospital with multiple osseous metastases. Four years previously she had a radical breast amputation for carcinoma. She had x-ray therapy after this operation. During a 14 weeks' stay in the hospital, she received 6 pints of blood. In another instance, a 77-year-old man was admitted to the hospital with severe anemia from carcinoma of the stomach. He received 5 units of blood but died 11 days after admission. Another man, aged 73, was admitted with carcinoma of the colon with metastases; he also had diabetes and hypertensive heart disease. He received 4 units of blood but died eight days after admission. Are blood transfusions indicated in such patients?*

M.D., Illinois.

Answer.—In this setting transfusions are considered as symptomatic or palliative treatment. Therefore, if the patient has symptoms reasonably attributable to anemia per se and if the anemia cannot be corrected by some other means, transfusions are indicated regardless of the patient's poor prognosis. Since the degree of anemia which will produce symptoms depends on the patient's activity and a number of other factors, the evaluation of the need for transfusion should be based on bedside observation rather than any arbitrary hemoglobin value. Patients with anemia due to disseminated cancer, not complicated by blood loss, characteristically have only a moderate anemia which is usually asymptomatic, particularly in those patients whose activity is limited. Most such patients, therefore, are not perceptibly benefited by transfusion. From these statements, it may be seen that the question of whether transfusion therapy was indicated in the cases cited cannot properly be evaluated without knowing more details of these patients' symptoms. It should be emphasized, however, that patients with incurable cancer deserve as careful and considerate symptomatic or palliative treatment as patients ill with non-neoplastic diseases.

LENSES FOR RETINITIS PIGMENTOSA

To the Editor:—*Will any type of lens allow vision from various parts of the retina in patients with retinitis pigmentosa?*

O. C. Amstutz, M.D., Irvine, Ky.

Answer.—There are no lenses especially designed or particularly adaptable for patients with retinitis pigmentosa. Lens systems are designed for eyes that have unusual optical disorders that cannot be corrected by single-piece lenses such as are worn in the usual spectacle frame. The result is an enlarged image on the retina that is helpful in patients with central retinal defects in providing vision in ordinary light. In persons with retinitis pigmentosa, central vision usually remains after peripheral areas of the retina become insensitive to light; consequently, an enlarged image does not materially improve vision. Colored lenses are helpful only in reducing glare or protecting the diseased and impoverished retinal elements from excessive light. The qualified answer to the question is "no."

FEATHERS AND SCALES

To the Editor:—*Prof. P. E. Raymond (Prehistoric Life, Cambridge, Mass., Harvard University Press, 1939, p. 184) has stated: "The scales in fish and the feathers in birds arise from different layers of the skin." Is this correct?*

John R. Howitt, M.D.
Port Arthur, Ontario, Canada.

Answer.—Professor Raymond's statement is correct. Earlier descriptions in comparative anatomy often created artificial series of analogous rather than homologous structures. Fish scales, whether of shark, sturgeon, or trout (placoid, ganoid, or cycloid types of scales, respectively) are derivatives of the dermis. The epidermis of fishes is very thin and never cornifies, and the scales remain embedded in the dermis. In sharks the teeth are modified scales. During the development of a feather there is a transitory dermal papilla which degenerates into the nonliving pulp. Barb and barbules originate entirely from epidermal cell columns which cornify. A feather, therefore, represents a complex

modification of the epidermis. The presence of a dermal papilla during the development of fish scales and of feathers probably led to the mistaken identification of such structures. Even a down feather is not an "elongated and frayed out scale."

Scales of reptiles and those on the legs of birds, however, are of epidermal origin. In these animals they represent a thickened stratum corneum and more nearly resemble feathers than do the scales of fishes.

INDURATED SCAR

To the Editor:—*About six weeks ago, a 14-year-old boy received a minor bruise in his upper lip. There was some exudation and slight bleeding at the time, but in a week all external evidence of the injury disappeared. There is, however, a definite area of scar tissue, flat and pea-sized in diameter, that has persisted in size and consistency. There is no possibility of foreign body. A similar scar was removed recently from another patient in the belief that it was a foreign body, but it recurred two weeks later. The scar tissue is not painful, but the boy is a capable cornetist and his teacher has advised him not to play his instrument or any other instrument involving the use of the lips until all evidence of this injury disappears. Is there anything that might speed his recovery?*

Louis H. Bos, M.D., Rehoboth, N. Mex.

Answer.—From the description given there was no evidence of a break in the skin of the upper lip. If there was such a break, the wound has apparently healed by secondary intention, leaving a scar both on the skin surface and in the subcutaneous tissue. It is not uncommon for such a scar to continue to be felt for three to six months after all external evidence of injury has disappeared. Some people are more subject to hypertrophic scarring than others. The softening of the scar might be hastened in its early stages by gentle massage with some such substance as cold cream or cocoa butter. It is questionable whether such a procedure would be of any value at this late stage, but the scar should become soft in time, permitting the boy to return to his cornet playing.

CORAL POISONING

To the Editor:—*What is the cause and treatment of "coral poisoning" (infected abrasions from coral)?*

D. D. Dieter, M.D., Eustis, Fla.

Answer.—Coral cuts are generally the result of brushing against or carelessly handling the sharp exoskeletons of various species of stony corals—members of the Coelenterata, order Anthozoa. The severity of the lesion depends on such factors as degree of laceration of the skin, introduction of foreign substances into the wound, venom from the stinging tentacles of the coral polyp, and secondary bacterial infection. Treatment consists of prompt cleansing of the wound, removal of foreign particles, débridement if necessary, and application of antiseptic agents. In severe cases it may be necessary to give the patient bed rest with elevation of the limb, kaolin poultices, dressings of magnesium sulfate in glycerin solution, and antibiotics. A detailed discussion of coral cuts is given by Halsted (Dangerous Marine Animals, Cambridge, Md., Cornell Maritime Press, 1958).

TRACHEAL SCLEROMA

To the Editor:—*What is the latest treatment for scleroma of the subglottic area of the trachea?*

Phelps P. Luria, M.D., Far Rockaway, N. Y.

Answer.—Scleroma is a chronic granulomatous disease which may affect any part of the respiratory tract. The diagnosis is based on cultures and biopsy specimens revealing the Fritsch bacillus (Klebsiella rhinoscleromatis), Russell's bodies (nonspecific eosinophilic masses thought to represent degenerated plasma cells), and the characteristic Mikulicz's cells (foamy abundant pale cytoplasm with a relatively small nucleus). Subglottic infiltration in scleroma may cause respiratory obstruction. Tracheostomy may be necessary if removal of the offending tissue does not alleviate respiratory embarrassment. In the active phase of the disease, treatment with tetracyclines or streptomycin is the current method of choice and represents a notable improvement over previous symptomatic measures. Cessation of activity in scleroma is often followed by scarring and stenosis of the larynx or upper trachea. Under these circumstances it is feasible to restore the lumen by removal of scar tissue and to insert a skin graft which can be maintained in position by some type of mold until healing has taken place.

SMALLPOX VACCINATION AND TUBERCULOSIS

To the Editor:—*Please give information on the effect of smallpox vaccination on undiagnosed primary tuberculosis of infancy.*

E. P. Dale, M.D., Los Angeles.

Answer.—There seems to be no valid contraindication to smallpox vaccination in undiagnosed (or diagnosed) primary tuberculosis in infancy. If there were a concealed risk in this situation it should have been well demonstrated by experience. It was formerly the custom in many communicable disease hospitals to vaccinate all patients on admission. In countries where both smallpox and tuberculosis are prevalent, smallpox vaccination is currently performed without reference to preexisting tuberculosis. In neither situation is there any evidence that vaccinia accelerates the tuberculous process. In the United States, under current con-

ditions the time of vaccination is an elective matter and the infant should be vaccinated when he is in normal health, but there is no reason to fear the existence of undiscovered primary tuberculosis.

TESTS FOR SPINAL FLUID LOSS

To the Editor:—*Please give a list of tests and references for the identification of spinal fluid escaping through basal skull fractures and the nose. Also, please outline the advantages and disadvantages of spinal injections of methylene blue as a test for such a fracture.*

Joseph Catton, M.D., San Francisco.

Answer.—Grossly, especially when the patient leans forward, a clear, odorless fluid in quantity may be collected in a test tube. No sediment is evident on standing. The specific gravity is between 1.005 and 1.010. The normal sugar content of the cerebrospinal fluid of fasting persons is between 50 and 80 mg.%. It is necessary only to demonstrate the reduction of copper sulfate in the collected fluid. The collected fluid will contain no mucin or albumin and only an occasional lymphocyte. It is possible to demonstrate the location of a fracture in the cribriform plate by the injection of 3 to 5 cc. of a 0.6% solution of indigo carmine into the spinal canal. A bluish green fluid will make its appearance in the nasal discharge within 10 to 15 minutes.

ALLERGY TO PENICILLINASE

To the Editor:—*A question and answer on allergy to penicillinase appeared in* The Journal, *Dec. 20, 1958, page 2207. I initiated the original in vivo and clinical studies pertaining to the use of penicillinase in the treatment of penicillin reactions. It is true, since penicillinase is a protein, that allergic reactions may occur after repeated injections of the enzyme, but when repeated injections are needed they are given over a short period during treatment of the penicillin reaction and there would not be time enough for antibodies to develop which would produce an immediate allergic reaction. If a patient received a further injection or injections of the enzyme months later, then a true allergic reaction might become manifest. The reactions to penicillinase referred to in the answer (including fever and chills), which has been described by me as well as by Zimmerman, cannot be classified as allergic. To my knowledge, about six such reactions occurred in about 300 treated patients. This represents more of a Herxheimer type of reaction, but it is still a mysterious entity.*

Regarding the time factor in using penicillinase in immediate reactions to penicillin, it may be said that within 15 minutes after an intramuscular injection of penicillinase no circulating penicillin can be detected and this would hold even for a shorter period if the enzyme is injected intravenously. If a patient dies within a minute or so after receiving penicillin one would mechanically be unable to get the enzyme into the patient in time, but in many immediate reactions patients go into shock and may be maintained with epinephrine and pressure substances for many hours. In this situation penicillinase can be lifesaving by immediately destroying the offending antigen. Concerning the last sentence, that penicillinase "may be of value in delayed reactions," it can be said that it has proved to be of great value in delayed reactions. In many patients the results have been nothing short of dramatic. In two patients with complete anuria for days associated with a penicillin reaction with no response to conventional means of treatment, marked diuresis began as soon as four hours after the injection of penicillinase.

Robert M. Becker, M.D.
3414 Monroe St.
Madison, Wis.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*Nothing in the original reply contradicts the correspondent's statement that allergic reactions to penicillinase might develop primarily after repeated injections, and nothing was said to contradict the opinion that the febrile reactions are not allergic. The acute anaphylactic symptoms produced by penicillin are produced by the sudden release of excessive amounts of histamine or other mediators responsible for the shock symptoms. This is the result of antigen-antibody union. After such a release one could presumably destroy all remaining penicillin and yet not prevent a fatal outcome, because the mediators already released are responsible for the shock. The major problem there is to counteract the effect of these mediators (such as with vasodilatation and bronchial constriction) and later to give medication to make the mediators, particularly histamine, inactive by administering antihistamine. This consultant has no objection to the use of penicillinase as long as the physician does not get the impression that it is the first line of procedure in combating anaphylaxis. Epinephrine, aminophylline, and antihistamine, in that order, are far more important. The correspondent takes issue with the use of the term "may." Does he claim that it is of value in all patients with delayed penicillin reactions? If so, both the published reports and my own experience contradict that contention. The fact remains that penicillinase may or may not be of value in treating delayed reactions.*